### Connecting via Winsock to STN

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Welcome to STN International! Enter x:x
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LOGINID: SSSPTA1613SXW

PASSWORD:

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Welcome to STN International
                 Web Page URLs for STN Seminar Schedule - N. America
NEWS
NEWS
         Apr 08
                 "Ask CAS" for self-help around the clock
NEWS
         Jun 03
                 New e-mail delivery for search results now available
NEWS
     4 Aug 08
                 PHARMAMarketLetter(PHARMAML) - new on STN
                 Aquatic Toxicity Information Retrieval (AQUIRE)
NEWS
         Aug 19
                 now available on STN
                 Sequence searching in REGISTRY enhanced
NEWS
         Aug 26
         Sep 03
                 JAPIO has been reloaded and enhanced
NEWS
      7
         Sep 16
                 Experimental properties added to the REGISTRY file
NEWS 8
                 CA Section Thesaurus available in CAPLUS and CA
NEWS 9
         Sep 16
NEWS 10
         Oct 01
                 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11
         Oct 24
                 BEILSTEIN adds new search fields
NEWS 12
         Oct 24
                 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13 Nov 18
                DKILIT has been renamed APOLLIT
NEWS 14 Nov 25
                More calculated properties added to REGISTRY
NEWS 15
        Dec 04
                 CSA files on STN
NEWS 16 Dec 17
                 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17
         Dec 17
                 TOXCENTER enhanced with additional content
NEWS 18
         Dec 17
                 Adis Clinical Trials Insight now available on STN
NEWS 19
         Jan 29
                 Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
                 CANCERLIT is no longer being updated
NEWS 20
         Feb 13
NEWS 21
         Feb 24
                 METADEX enhancements
NEWS 22
         Feb 24
                 PCTGEN now available on STN
NEWS 23
         Feb 24
                 TEMA now available on STN
NEWS 24
         Feb 26
                 NTIS now allows simultaneous left and right truncation
NEWS 25
         Feb 26
                 PCTFULL now contains images
NEWS 26
        Mar 04
                 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27
         Mar 19
                 APOLLIT offering free connect time in April 2003
NEWS 28
         Mar 20
                 EVENTLINE will be removed from STN
NEWS 29
         Mar 24
                 PATDPAFULL now available on STN
NEWS 30
         Mar 24
                 Additional information for trade-named substances without
                 structures available in REGISTRY
                 Display formats in DGENE enhanced
NEWS 31
         Apr 11
NEWS 32
                 MEDLINE Reload
         Apr 14
NEWS 33
                 Polymer searching in REGISTRY enhanced
         Apr 17
NEWS 34
                 Indexing from 1947 to 1956 being added to records in CA/CAPLUS
         Apr 21
         Apr 21
NEWS 35
                 New current-awareness alert (SDI) frequency in
                 WPIDS/WPINDEX/WPIX
NEWS 36
                 RDISCLOSURE now available on STN
         Apr 28
NEWS 37
                 Pharmacokinetic information and systematic chemical names
         May 05
                 added to PHAR
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NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 14:41:35 ON 08 MAY 2003

=> fil reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:41:43 ON 08 MAY 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAY 2003 HIGHEST RN 511508-58-0 DICTIONARY FILE UPDATES: 6 MAY 2003 HIGHEST RN 511508-58-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

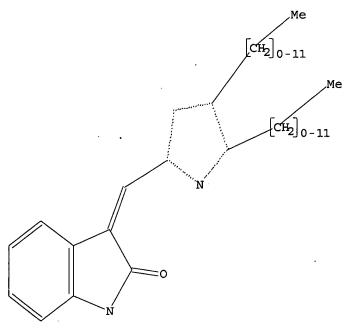
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> Uploading 09897755c.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11 sss sam

SAMPLE SEARCH INITIATED 14:42:08 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 59 TO ITERATE

100.0% PROCESSED 59 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 720 TO 1640

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 14:42:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1297 TO ITERATE

100.0% PROCESSED 1297 ITERATIONS 14 ANSWERS

SEARCH TIME: 00.00.01

L3 14 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST ENTRY SESSION 148.15 148.36

FILE 'CAPLUS' ENTERED AT 14:42:19 ON 08 MAY 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 8 May 2003 VOL 138 ISS 19 FILE LAST UPDATED: 7 May 2003 (20030507/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 full

10 L3 L4

=> d 14 1-10 ibib abs hitstr

ANSWER 1 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2000:500184 CAPLUS

DOCUMENT NUMBER:

133:234344

TITLE:

DOMCoSAR: A Novel Approach for Establishing the

Docking Mode That Is Consistent with the

Structure-Activity Relationship. Application to HIV-1 Protease Inhibitors and VEGF Receptor Tyrosine Kinase

Inhibitors

AUTHOR (S):

Vieth, Michal; Cummins, David J.

CORPORATE SOURCE:

Lilly Research Laboratories, Eli Lilly and Company,

Indianapolis, IN, 46285, USA

SOURCE: .

Journal of Medicinal Chemistry (2000), 43(16),

3020-3032

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE: English

DoMCoSAR is a novel approach for statistically detg. the docking mode that is consistent with a structure-activity relationship. The approach establishes the binding mode for the compds. in a chem. series with the assumption that all mols. exhibit the same binding mode. It involves three stages. In the first stage all mols. that belong to a given chem. series are docked to the active site of the protein target. The only bias used in the docking at this stage involves the location of the protein binding site. Coordinates of the common substructure (CS) that results from the unbiased docking are then clustered to establish the major substructure docking modes. In the second stage all mols. are docked to the major docking modes (MDMs) with constraints based on the common substructure. The third stage generates, for the major docking modes, interaction-based descriptors that include electrostatic, VDW, strain, and solvation contributions. The problem of docking mode evaluation is now reduced to the question of which descriptor set is more predictive. To

establish a quant. comparison of the descriptor sets assocd. with the major docking modes, we use 50 instances of random 4-fold cross-validation. For each 4-fold cross-validation the predictive squared correlation coeff. (R2) is computed. T-Tests are applied to establish significance of the differences in mean R for one docking mode vs. another. We test the methodol. on two test cases: HIV-1 protease inhibitors (Holloway et al. J. Med. Chem. 1995, 38, 305-317) and vascular endothelial growth factor (VEGF) receptor tyrosine kinase oxoindoles (Sun et al. J. Med. Chem. 1998, 41, 2588-2603). For both test cases there is statistically significant preference for the binding mode consistent with the x-ray structure. The appeal of this methodol. is that researchers gain the objectivity of statistical justification for the selected docking mode. The methodol is relatively insensitive to subtle variations of the protein structure that include, but are not limited to, side chain and small backbone rearrangement during binding. In addn., predictive models that result from the approach can be used to further optimize chem. series.

IT 186611-29-0 186611-48-3

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(VEGF kinase-inhibitor; DoMCoSAR - novel approach for establishing docking mode that is consistent with structure-activity relationship with application to HIV-1 protease inhibitors and VEGF receptor tyrosine kinase inhibitors)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1999:205317 CAPLUS

DOCUMENT NUMBER: 130:252240

TITLE: Preparation of 3-benzylidene-2-indolinones as tyrosine

kinase activity modulators

INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: U.S., 40 pp., Cont.-in-part of U.S. Ser. No. 485,323.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

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EP	934931	A2	19990811		ΕP	199	9-10	366	7	1996	0605			
· EP	934931		19991020											
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	IE, SI,	-						,		,	•		•	
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US	2002102608	A1	20020801		US	200	1-89	7755	5	2001	0703			
US	2003069421									2002				
PRIORITY	Y APPLN. INFO	. :		US	199	5-4	8532	23	A2	1995	0607			
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				JP	199	7-5	0136	53	Α3	1996	0605			
				US	199	6-6	5522	23	A2	1996	0605			
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				US	199	6-6	5522	26	A2	1996	0605			
				US	199	6-6	5525	55	B2	1996	0605			
				US	199	6-6	5919	91	A2	1996	0605			
•				US	199	6-7	0223	32	В1	1996	0823			
		•	•	US	199	7-9	1536	56	А3	1997	0820			

MARPAT 130:252240

US 1998-75271

B1 19980508

OTHER SOURCE(S):

GI

AB Title compds. [I; R1 = H or alkyl; R3 = ZR2; R2 = OR, NRaRb, 5-membered heteroaryl, etc.; R = H, alkyl, aryl; Ra,Rb = H, alkyl, COR; NRaRb = heterocyclyl; R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S; Z = (un)substituted 1,4-phenylene] were prepd. Thus, 2-oxindole was condensed with PhCHO to give 3-benzylidene-2-indolinone. Data for biol. activity of

I were given.

IT 186610-95-7P 186611-29-0P 186611-48-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-benzylidene-2-indolinones as tyrosine kinase activity modulators)

RN 186610-95-7 CAPLUS

CN 2H-Indol-2-one, 3-[(4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1999:193848 CAPLUS

DOCUMENT NUMBER:

130:237471

TITLE:

3-(2-Alkoxybenzylidene)-2-indolinones and their

analogs for the treatment of disease

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 485,323. SOURCE:

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ----Α US 5883116 19990316 US 1996-655224 19960605 US 5880141 Α 19990309 US 1995-485323 19950607 CA 2192797 CA 1996-2192797 AΑ 19961219 19960605 EP 934931 EP 1999-103667 A2 19990811 19960605

EP 934931 Α3 19991020

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI

JP 2000026412 JP 1999-159567 19960605 A2 20000125 ES 2159741 T3 ES 1996-918093 19960605 20011016 JP 3231044 B2 20011119 JP 1997-501363 19960605 US 2002022626 US 2000-617529 Α1 20020221 20000713 US 2002102608 US 2001-897755 Α1 20020801 20010703

PRIORITY APPLN. INFO.:

US 1995-485323 A2 19950607 A3 19960605 EP 1996-918093 JP 1997-501363 A3 19960605 US 1996-655223 A2 19960605 US 1996-655224 A2 19960605 US 1996-655226 A2 19960605 US 1996-655255 B2 19960605 US 1996-659191 A2 19960605

US 1996-702232 B1 19960823 US 1997-915366 A3 19970820

OTHER SOURCE(S):

MARPAT 130:237471

GT

Indolinones such as I were prepd. for modulating tyrosine kinase signal AB transduction in order to regulate, modulate, and/or inhibit abnormal cell proliferation. Thus, a mixt. of 134.0 mg oxindole, 151.4 mg 3-methyl-2-thiophenecarboxaldehyde, and 3 drops of piperidine in 2 mL EtOH was stirred at 90.degree. for 3 h to give a 65% yield of I. In an ELISA assay to measure the inhibition of protein tyrosine kinase activity on the FLK-1 receptor, I showed an IC50 of 4.5 .mu.M.

ΙT 186611-29-0P, SU 5453 186611-48-3P, SU 5477

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(3-(2-alkoxybenzylidene)-2-indolinones and their analogs for modulating tyrosine kinase signal transduction)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:193846 CAPLUS

DOCUMENT NUMBER:

130:237470

TITLE:

Preparation of 3-benzylidene-2-indolinones as tyrosine

kinase activity modulators

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 485,233.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5883113 ·	Α	19990316	US 1996-659191	19960605
US 5880141	Α	19990309	US 1995-485323	19950607
CA 2192797	AA	19961219	CA 1996-2192797	19960605
EP 934931	A2	19990811	EP 1999-103667	19960605
EP 934931	<b>A</b> 3	19991020		
R: AT, BE,	CH, DE	, DK, ES, FR,	GB, GR, IT, LI, LU	, NL, SE, MC, PT,
IE, SI,	LT, LV	, FI		
JP 2000026412	A2	20000125	JP 1999-159567	19960605

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ES 1996-918093
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PRIORITY APPLN. INFO.:
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                                          US 1996-659191
                                                            A1 19960605
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                                          US 1998-212494
                                                            A2 19981215
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OTHER SOURCE(S):

MARPAT 130:237470

AB Title compds. [I; R1 = H or alkyl; R3 = ZR2, 5-membered heteroaryl, etc.; R2 = OR, NRaRb, etc.; R = H, alkyl, aryl, etc.; Ra,Rb = H, alkyl, COR, etc.; NRaRb = heterocyclyl; R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S; Z = (un)substituted 1,4-phenylene] were prepd. Thus, PhCHO was condensed with 2-oxindole to give I (R1 = R4-R7 = H, R3 = Ph, X = O). Data for biol. activity of I were given.

IT 186611-29-0P, SU 5453 186611-48-3P, SU 5477
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-benzylidene-2-indolinones as tyrosine kinase activity
 modulators)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 56

THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:747592 CAPLUS

DOCUMENT NUMBER:

130:3771

TITLE:

Preparation of 3-(hetero)arylmethylidene-2-indolinone

derivatives as modulators of protein kinase activity

for use in treating cancer.

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald; Shawver,

Laura Kay; Hirth, Klaus Peter

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 269 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO	9850	356		A:	1	1998	1112		W	O 199	98-U	5901	7 :	1998	0507		
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	•	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
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		CM,	GA,	GN,	ML,	MR,	NE,	SN,	TD,	TG							
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US	6051	593 <sup>°</sup>		Α	;	2000	0418		U	S 199	98-99	9721	:	19980	0619		

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					US	1997-59677P	P	19970919
					US	1997-59971P	P	19970925
					US	1997-60194P	P	19970926
					WO	1998-US9017	W	19980507
					US	1998-100854	A3	19980619
		•			US	1998-99721	<b>A1</b>	19980619
					US	1998-161046	<b>A</b> 3	19980925
					US	2000-482198	<b>A</b> 3	20000112
		•			US	2000-516948	В1	20000301

OTHER SOURCE(S):

MARPAT 130:3771

$$\begin{array}{c|c}
R^{4} & R^{2} \\
R^{4} & A^{2} \\
R^{5} & A^{4} \\
R^{6} & R^{1}
\end{array}$$

Ι

AB Title compds. [I; A1-A4 = C, N; when any of A1-A4 = N, then the
 corresponding R3-R6 = null; R1 = H, alkyl, cycloalkyl, alkenyl, alkynyl,
 aryl, heteroaryl, heteroalicyclyl, trihalomethylcarbonyl, OH, CO2H,
 trihalomethylsulfonyl, etc.; R2 = H, alkyl, cycloalkyl, aryl, heteroaryl,
 heteroalicyclyl, halo; R3-R6 = H, alkyl, trihalomethyl, cycloalkyl,
 alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclyl, OH, SH, alkoxy,
 aryloxy, amino, phosphonyl, guanidinyl, NO2, halo, (iso)cyanato, etc.;
 R3R4 or R4R5 or R5R6 = cycloalkyl, aryl, heteroaryl, heteroalicyclyl,
 OCH2O, OCH2CH2O; Q = specified (substituted) (hetero)aryl; Z = O, S], were
 prepd. Thus, 3-(4-imidazolylmethylidenyl)-4,6-dimethyl-2-indolinone
 inhibited CDK2 with IC50 = <0.78 .mu.M.</pre>

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

CN

(prepn. of 3-(hetero)arylmethylidene-2-indolinone derivs. as modulators of protein kinase activity for use in treating cancer)

RN215537-01-2 CAPLUS

> 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

Br Me Et Me

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS

1

ACCESSION NUMBER:

1998:735056 CAPLUS

DOCUMENT NUMBER:

129:330650

TITLE:

Preparation of 3-benzylidene-2-indolinones and analogs

as tyrosine kinase signal transduction modulators

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S):

Sugen Inc., USA

SOURCE:

U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 485,323.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE			
			'				
US 5834504	Α	19981110	US 1996-655225	19960605			
US 5880141	A	19990309	US 1995-485323	19950607			
CA 2192797	AA	19961219	CA 1996-2192797	19960605			
EP 934931	A2	19990811	EP 1999-103667	19960605			
EP 934931	A3	19991020					
R: AT, BE,	CH, DE,	DK, ES,	FR, GB, GR, IT, LI, LU,	NL, SE, MC, PT,			
IE, SI,	LT, LV,	FI					
JP 2000026412	A2	20000125	JP 1999-159567	19960605			
ES 2159741	T3	20011016	ES 1996-918093	19960605			
JP 3231044	B2	20011119	JP 1997-501363	19960605			
US 2002022626	A1	20020221	US 2000-617529	20000713			
PRIORITY APPLN. INFO	. :		US 1995-485323 A2	19950607			
			EP 1996-918093 A3	19960605			
			JP 1997-501363 A3	19960605			
			US 1997-915366 A3	19970820			
OMITED COITE OF (C)	343 7			•			

OTHER SOURCE(S):

MARPAT 129:330650

GI

IT

AB Title compds. [I; R1 = H or alkyl; R2 = 2-halo-4-hydroxy- or -alkoxyphenyl, 4-hydroxy- or -alkoxyphenyl, 4-(di)(alkyl)aminophenyl, heteroaryl, etc.; R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S] were prepd. Thus, oxindole was condensed with 2-chloro-4-methoxybenzaldehyde to give I (R1 = R4-R7 = H, R2 = 2-chloro-4-methoxyphenyl, X = O). Data for biol. activity of I were given.

186611-29-0P 186611-48-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-benzylidene-2-indolinones and analogs as tyrosine kinase signal transduction modulators)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

181 THERE ARE 181 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1998:542764 CAPLUS

DOCUMENT NUMBER: 129:175549

TITLE: Preparation of 3-(hetero)arylmethylene-2-indolinones

as tyrosine kinase signal transduction modulators

INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 485,323.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PA	TENT NO.		DATE					DATE			
110	5792783	Δ	19980811	-		96-65		19960605			
110	5880141	7	1000011		110 10	05_40	5223	19950603			
03	2102707	A3.	10061010		05 15	06 21	00707	19950007			
CA	2192797 934931	. AA	19961219		CA 19	96-21	92191	19960605			
					EP 19	99-10	3667	19960605			
EP	934931										
	R: AT, BE				B, GR,	IT,	LI, LU	, NL, SE,	MC,	PT,	
	IE, SI	, LT, LV	, FI								
JP	2000026412	A2	20000125		JP 19	99-15	9567	19960605			
ES	2159741	T3	20011016		ES 19	96-91	8093	19960605			
JP	3231044	B2	20011119		JP 19	97-50	1363	19960605			
US	6316635	B1	20011113		US 19	99-29	3518	19990415			
US	2002022626	A1	20020221		US 20	00-61	7529	20000713			
US	2002102608	. A1	20020801		US 20	01-89	7755	20010703			
PRIORITY	Y APPLN. IN	·O.:		US	1995-	48532	3 A2	19950607			
				EF	1996-	91809	3 . A3	19960605			
				JF	1997-	50136	3 A3	19960605			
								19960605			
					1996-			19960605			
				US	1996-	65522	6 A2	19960605			
					1996-			19960605			
					1996-			19960605			
					1996-			19960823			
								19970820			
					1998-			19980416			
				US	T338-	21249	4 AZ	19981215			

OTHER SOURCE(S):

MARPAT 129:175549

$$R^{4}$$
 CHR<sup>2</sup>
 $R^{5}$ 
 $R^{6}$ 
 $R^{7}$ 
 $R^{1}$ 
 $R^{1}$ 

AB Title compds. [I; R1 = H or alkyl; R2 = (un)substituted (hetero)aryl; R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S] were prepd. Thus, oxindole was condensed with 4-pyridinecarboxaldehyde to give I (R1,R4-R7 = H, R2 = 4-pyridinyl, X = O). Data for biol. activity of I were given.

IT 186611-29-0P 186611-48-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 3-(hetero)arylmethylene-2-indolinones as tyrosine kinase signal transduction modulators)

RN186611-29-0 CAPLUS

2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-CN dihydro- (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3dihydro- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

179 THERE ARE 179 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2003 ACS ANSWER 8 OF 10 ACCESSION NUMBER:

DOCUMENT NUMBER:

1998:429042 CAPLUS 129:117426

TITLE:

Synthesis and Biological Evaluations of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase

Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases

AUTHOR (S):

Sun, Li; Tran, Ngoc; Tang, Flora; App, Harald; Hirth,

Peter; McMahon, Gerald; Tang, Cho

CORPORATE SOURCE:

SUGEN Inc, Redwood City, CA, 94063, USA

SOURCE:

Journal of Medicinal Chemistry (1998), 41(14),

2588-2603

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

3-Substituted indolin-2-ones have been designed and synthesized as a novel class of tyrosine kinase inhibitors which exhibit selectivity toward different receptor tyrosine kinases (RTKs). These compds. have been evaluated for their relative inhibitory properties against a panel of RTKs in intact cells. By modifying the 3-substituted indolin-2-ones, we have identified compds. which showed selective inhibition of the ligand-dependent autophosphorylation of various RTKs at submicromolar levels in cells. Structure-activity anal. for these compds. and their

relative potency and selectivity to inhibit particular RTKs has detd. that (1) 3-[(five-membered heteroaryl ring)methylidenyl]indolin-2-ones are highly specific against the VEGF (Flk-1) RTK activity, (2) 3-(substituted benzylidenyl)indolin-2-ones contg. bulky group(s) in the Ph ring at the C-3 position of indolin-2-ones showed high selectivity toward the EGF and Her-2 RTKs, and (3) the compd. contg. an extended side chain at the C-3 position of the indolin-2-one exhibited high potency and selectivity when tested against the PDGF and VEGF (Flk-1) RTKs. Recent published crystallog. data for two of these 3-substituted indolin-2-ones provides a rationale to suggest that these compds. may bind in the ATP binding pocket of RTKs. The structure-activity anal. supports the use of subsets of these compds. as specific chem. leads for the development of RTK-specific drugs with broad application for the treatment of human diseases.

IT 210303-53-0P 210303-55-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and evaluation of 3-substituted indolin-2-ones as inhibitors of selective growth factor receptors)

RN 210303-53-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 210303-55-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1998:147306 CAPLUS

DOCUMENT NUMBER: 128:204803

TITLE: Indolinone combinatorial libraries and related

products and methods for the treatment of disease

INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald; Hirth, Klaus

Peter; Shawver, Laura Kay; et al.

PATENT ASSIGNEE(S):

```
Gerald
SOURCE:
                       PCT Int. Appl., 293 pp.
                       CODEN: PIXXD2
                       Patent
DOCUMENT TYPE:
LANGUAGE:
                       English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:
                 KIND DATE
                                 APPLICATION NO. DATE
    PATENT NO.
    -----
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                                       -----
                   A1 19980226 WO 1997-US14736 19970820
    WO 9807695
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
            UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
            GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
            GN, ML, MR, NE, SN, TD, TG
    CN 1155838
                   A 19970730
                                      CN 1996-190616
                                      EP 1997-939480 19970820
    EP 929520
                    Al 19990721
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
           IE, FI
                                        US 1997-915366
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    JP 2001503736
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                                                        19970820
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    EP 1247803
                                       EP 2002-77564
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                     A2
    EP 1247803
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                    A3
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    US 2002022626
                     A1
                          20020221
                                                        20000713
PRIORITY APPLN. INFO.:
                                     US 1996-702232 A 19960823
                                     US 1996-31585P
                                                    P 19961205
                                                    P 19961205
                                     US 1996-31586P
                                     US 1996-31588P
                                                     P 19961205
                                     US 1996-32546P
                                                     P 19961205
                                     US 1996-32547P
                                                     P 19961205
                                     US 1997-45565P
                                                     P 19970505
                                    · US 1997-45566P
                                                     P 19970505
                                     US 1997-45714P
                                                     P 19970505
                                     US 1997-45715P
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                                                     P 19970505
                                     US 1996-45715P
                                                     P 19961205
                                     US 1997-31565P
                                                     P 19970505
                                     EP 1997-939480
                                                     A3 19970820
                                     US 1997-915366
                                                     A3 19970820
                                     WO 1997-US14736 W 19970820
                      MARPAT 128:204803
OTHER SOURCE(S):
GT
```

Sugen, Inc., USA; Tang, Peng Cho; Sun, Li; McMahon,

AB The invention relates to indolinone derivs. capable of modulating, regulating, and/or inhibiting protein kinase signal transduction. compds. are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK protein kinase can be obtained by adding chem. substituents to the 3-[(indole-3yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. Indolinone compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosol. indolinone compds. that are tyrosine kinase inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepd. by combinatorial condensation of certain (un) substituted indolinones with aldehydes at the 3-position. I gave complete inhibition of MET kinase at chimeric MET receptors in vitro. IT 203989-88-2P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone 203989-98-4P, 3-[(2,4-Dimethyl-3ethylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone 203990-08-3P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2indolinone 203990-18-5P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5y1) methylideny1] -5-[(methylamino) sulfony1] -2-indolinone 203990-28-7P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-38-9P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203990-48-1P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2indolinone 204005-38-9P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and testing of indolinone combinatorial library as protein kinase inhibitors) 203989-88-2 CAPLUS RNCN2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203989-98-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203990-08-3 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203990-18-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203990-28-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203990-38-9 CAPLUS

CN Morpholine, 4-[[3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203990-48-1 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 204005-38-9 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ N & CH & N \\ \end{array}$$
 Me Et

REFERENCE COUNT:

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2003 ACS .

ACCESSION NUMBER:

1997:140244 CAPLUS

DOCUMENT NUMBER:

126:139901

TITLE:

Indolinone compounds capable of modulating tyrosine

kinase signal transduction

SOURCE:

INVENTOR(S):

PATENT ASSIGNEE(S):

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DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                      KIND DATE
                                          APPLICATION NO. DATE
     WO 9640116
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                                           WO 1996-US8903
                                                             19960605
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             NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM,
             AZ, BY
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
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PRIORITY APPLN. INFO.:
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                                                         A3 19960605
                                        JP 1997-501363
                                                         A3 19960605
                                        WO 1996-US8903
                                                         W
                                                            19960605
                                        US 1997-915366
                                                         A3 19970820
OTHER SOURCE(S):
                         MARPAT 126:139901
    The present invention relates to org. mols. capable of modulating tyrosine
    kinase signal transduction in order to regulate, modulate and/or inhibit
    abnormal cell proliferation. Representatives of the 5 different classes
    of compds. described are SU 4932 [3-(2-chloro-4-hydroxybenzylidenyl)-2-
     indolinone], SU 4312 [3-(4-dimethylaminobenzylidenyl)-2-indolinone], SU
     5416 {3-[(2,4-dimethylpyrrol-5-yl)methylene]-2-indolinone}, SU 5204
     [3-(2-ethoxybenzylidenyl)-2-indolinone], and SU 4942 [3-(4-
    bromobenzylidenyl)-2-indolinone]. Diseases which these compds. and their
    pharmaceutically acceptable prepns. may be effective against include
    arthritis, hepatic cirrhosis, diabetic nephropathy and psoriasis.
IT
    186611-29-0P, SU 5453 186611-48-3P, SU 5477
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
```

Tang, Peng Cho; Sun, Li; Mcmahon, Gerald

Sugen, Inc., USA

CODEN: PIXXD2

PCT Int. Appl., 133 pp.

BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of indolinones capable of modulating tyrosine kinase signal transduction)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

## Connecting via Winsock to STN

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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     3
NEWS
         Aug 08
                 PHARMAMarketLetter(PHARMAML) - new on STN
                 Aquatic Toxicity Information Retrieval (AQUIRE)
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                 JAPIO has been reloaded and enhanced
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         Sep 03
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         Sep 16
                 Experimental properties added to the REGISTRY file
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         Sep 16
                 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 10
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        Oct 24 BEILSTEIN adds new search fields
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NEWS 12
         Oct 24
                Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13
         Nov 18
                DKILIT has been renamed APOLLIT
NEWS 14
        Nov 25
                 More calculated properties added to REGISTRY
NEWS 15
                 CSA files on STN
        Dec 04
        Dec 17
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                 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17
         Dec 17
                 TOXCENTER enhanced with additional content
NEWS 18
         Dec 17
                 Adis Clinical Trials Insight now available on STN
NEWS 19
         Jan 29
                 Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
NEWS 20
         Feb 13
                 CANCERLIT is no longer being updated
         Feb 24 METADEX enhancements
NEWS 21
NEWS 22
         Feb 24
                 PCTGEN now available on STN
NEWS 23
        Feb 24
                 TEMA now available on STN
        Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 24
NEWS 25
        Feb 26
                PCTFULL now contains images
NEWS 26 Mar 04
                 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27
        Mar 19 APOLLIT offering free connect time in April 2003
NEWS 28 Mar 20
                 EVENTLINE will be removed from STN
NEWS 29
         Mar 24
                 PATDPAFULL now available on STN
NEWS 30
        Mar 24
                 Additional information for trade-named substances without
                 structures available in REGISTRY
                 Display formats in DGENE enhanced
NEWS 31
         Apr 11
                 MEDLINE Reload
NEWS 32
         Apr 14
                 Polymer searching in REGISTRY enhanced
NEWS 33
         Apr 17
                 Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34
         Apr 21
NEWS 35
         Apr 21
                 New current-awareness alert (SDI) frequency in
                 WPIDS/WPINDEX/WPIX
                 RDISCLOSURE now available on STN
NEWS 36
        Apr 28
                 Pharmacokinetic information and systematic chemical names
NEWS 37
        May 05
                 added to PHAR
```

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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FULL ESTIMATED COST

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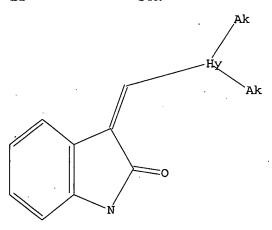
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS Ll STR



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=> s 11 sss sam

SAMPLE SEARCH INITIATED 16:02:20 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 3611 TO ITERATE

27.7% PROCESSED 1000 ITERATIONS 17 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

68618 TO 75822 757 TO

1697

PROJECTED ANSWERS:

17 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 16:02:23 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 73085 TO ITERATE

100.0% PROCESSED 73085 ITERATIONS 1549 ANSWERS

SEARCH TIME: 00.00.02

L3

L2

1549 SEA SSS FUL L1

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FILE COVERS 1907 - 8 May 2003 VOL 138 ISS 19 FILE LAST UPDATED: 7 May 2003 (20030507/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 full

121 L3 L4

=> d 14 111-121 ibib abs hitstr

ANSWER 111 OF 121 CAPLUS COPYRIGHT 2003 ACS

1998:735056 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 129:330650

Preparation of 3-benzylidene-2-indolinones and analogs TITLE:

as tyrosine kinase signal transduction modulators

Tang, Peng Cho; Sun, Li; McMahon, Gerald INVENTOR(S):

Sugen Inc., USA PATENT ASSIGNEE(S):

U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 485,323. SOURCE:

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE	
US 5834504	Α	19981110	US 1996-655225 19960605	
US 5880141	Α	19990309	US 1995-485323 19950607	
CA 2192797	AA	19961219	CA 1996-2192797 19960605	
EP 934931	A2	19990811	EP 1999-103667 19960605	
EP 934931	A3	19991020		
R: AT, BE,	CH, DE	, DK, ES, FF	R, GB, GR, IT, LI, LU, NL, SE, MC,	PT,
. IE, SI,	LT, LV	, FI		
JP 2000026412	A2	20000125	JP 1999-159567 19960605	
ES 2159741	Т3	20011016	ES 1996-918093 19960605	
JP 3231044	B2	20011119	JP 1997-501363 19960605	
US 2002022626	<b>A1</b>	20020221	US 2000-617529 20000713	
PRIORITY APPLN. INFO	. :		US 1995-485323 A2 19950607	
			EP 1996-918093 A3 19960605	
			JP 1997-501363 A3 19960605	
•			US 1997-915366 A3 19970820	

OTHER SOURCE(S): MARPAT 129:330650

AB Title compds. [I; R1 = H or alkyl; R2 = 2-halo-4-hydroxy- or -alkoxyphenyl, 4-hydroxy- or -alkoxyphenyl, 4-(di)(alkyl)aminophenyl, heteroaryl, etc.; R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S] were prepd. Thus, oxindole was condensed with 2-chloro-4-methoxybenzaldehyde to give I (R1 = R4-R7 = H, R2 = 2-chloro-4-methoxyphenyl, X = O). Data for biol. activity of I were given.

IT 15966-93-5P 186610-94-6P 186611-14-3P 186611-16-5P 186611-29-0P 186611-30-3P 186611-31-4P 186611-37-0P 186611-39-2P 186611-48-3P 204005-03-8P 204005-46-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-benzylidene-2-indolinones and analogs as tyrosine kinase signal transduction modulators)

RN 15966-93-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-94-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-16-5 CAPLUS
CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-29-0 CAPLUS
CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-30-3 CAPLUS
CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl es

ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 CAPLUS
CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline & N & O \\ \hline & CH & M & C-OEt \\ \hline & O & O \\ \hline & & & \\ EtO-C-CH_2-CH_2 & CH_2-C-OEt \\ \hline \end{array}$$

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-03-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & CH & N & \\ \hline & CH_2-CH_2-C-OMe \\ \end{array}$$

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

181 THERE ARE 181 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 112 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:685118 CAPLUS

DOCUMENT NUMBER:

129:310905

TITLE:

Study and treatment of diseases related to specific

cellular functions of receptor protein tyrosine

kinases

INVENTOR (S):

Clary, Douglas Sugen, Inc., USA

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	PATENT NO.				KIND DATE				APPLICATION NO. DATE									
W	0	9845	708		 A	1	1998:	1015		Ţ	NO 19	98-U	 S684:	- <del>-</del> 2	1998	0407		
		W:	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG	, BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
			DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM	, GW,	HU,	ID,	IL,	IS,	JP,	KE,	KG,
			ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT	, LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
			NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE	, SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,
			UA,	ŬĠ,	US,	UZ,	VN,	YU,	ZW,	AM	, AZ,	BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM
		RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	UG	, ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
			FI,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC.	, NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
			CM,	GΑ,	GN,	ML,	MR,	NE,	SN,	TD.	, TG					•		
ΑU	IJ	98688	376		A:	1	1998:	1030		Ī	AU 19	98-6	8876		1998	0407		
US	S	20020	0683	51	A:	1	2002	0606		τ	JS 19	98-5	7150		1998	0407		
US	S	62357	769		B	l	2001	0522		τ	JS 19	98-1	0988	3	1998	0702		
PRIORIT	ΓY	APPI	LN.	INFO.	. :				Ţ	US :	1997-	4320	7 P	P	1997	0408		
									τ	US :	1997-	5171	5P	P	1997	0703		

WO 1998-US6842 W 19980407

AB The invention relates to methods of evaluating the specific function of a receptor protein tyrosine kinase in cells by activating the receptor in a ligand-independent fashion. In addn., the invention includes methods of identifying compds. that modulate receptor protein tyrosine kinase function. The invention also relates to a method of preventing or treating an abnormal condition caused by an aberration in the function of the C-RET receptor, and specifically to the treatment and prevention of neurodegenerative disorders by administering a compd. that modulates the function of the C-RET receptor.

IT 204003-90-7 204003-91-8 204003-96-3 204003-97-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(study and treatment of diseases related to specific cellular functions of receptor protein tyrosine kinases, and screening method)

RN 204003-90-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-91-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-96-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-97-4 CAPLUS

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)

$$HO_2C-CH_2-CH_2$$
 $HO_2C-CH_2-CH_2$ 
 $HO_2C-CH_2-CH_2$ 
 $HO_2C-CH_2-CH_2$ 
 $HO_2C-CH_2-CH_2$ 

REFERENCE COUNT:

8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 113 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:542764 CAPLUS

DOCUMENT NUMBER:

129:175549

TITLE:

Preparation of 3-(hetero)arylmethylene-2-indolinones as tyrosine kinase signal transduction modulators

INVENTOR(S): Tang, Peng Cho; Sun, Li; McMahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

U.S., 37 pp., Cont.-in-part of U. S. Ser. No. 485,323.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE	
US 5792783	Α	19980811	US 1996-655223 19960605	
US 5880141	Α	19990309	US 1995-485323 19950607	
CA 2192797	AA	19961219	CA 1996-2192797 19960605	
EP 934931	A2	19990811	EP 1999-103667 19960605	
EP 934931	A3	19991020		
R: AT, BE,	CH, DE	, DK, ES,	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,	
IE, SI,				
JP 2000026412	A2	20000125	JP 1999-159567 19960605	
ES 2159741	T3	20011016	ES 1996-918093 19960605	
JP 3231044	B2	20011119	JP 1997-501363 19960605	
US 6316635	B1	20011113	US 1999-293518 19990415	
US 2002022626	A1	20020221	US 2000-617529 20000713	
US 2002102608	<b>A1</b>	20020801	US 2001-897755 20010703	
PRIORITY APPLN. INFO	. :		US 1995-485323 A2 19950607	
			EP 1996-918093 A3 19960605	
			JP 1997-501363 A3 19960605	
			US 1996-655223 A2 19960605	
			US 1996-655224 A2 19960605	
			US 1996-655226 A2 19960605	
			US 1996-655255 B2 19960605	
			US 1996-659191 A1 19960605	
			US 1996-702232 B1 19960823	
•			US 1997-915366 A3 19970820	•
			US 1998-82056P P 19980416	
			US 1998-212494 A2 19981215	
OTHER COURCE/C)	M7\1	ייסטר שעמם.	175540	

OTHER SOURCE(S):

MARPAT 129:175549

GI

Title compds. [I; R1 = H or alkyl; R2 = (un)substituted (hetero)aryl; AΒ R4-R7 = H, halo, alkyl, alkoxy, etc.; X = O or S] were prepd. Thus, oxindole was condensed with 4-pyridinecarboxaldehyde to give I (R1,R4-R7 = H, R2 = 4-pyridinyl, X = 0). Data for biol. activity of I were given. 15966-93-5P 186610-94-6P 186611-14-3P IT 186611-16-5P 186611-17-6P 186611-29-0P 186611-30-3P 186611-31-4P 186611-37-0P 186611-39-2P 186611-48-3P 186611-56-3P 186611-67-6P 204005-46-9P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 3-(hetero)arylmethylene-2-indolinones as tyrosine kinase signal transduction modulators) RN15966-93-5 CAPLUS 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-CN

ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186610-94-6 CAPLUS CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 186611-16-5 CAPLUS

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN - 186611-30-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester

(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O \\ \hline & H & \parallel \\ CH & C-OEt \\ \hline & CH_2 & CH_2-CH_2-C-OEt \\ \hline & CH_2-CH_2-C-OET \\ \hline \end{array}$$

RN 186611-31-4 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & N & Me & Et \end{array}$$

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-67-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT:

179 THERE ARE 179 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

ANSWER 114 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:429042 CAPLUS

DOCUMENT NUMBER: 129:117426

TITLE: Synthesis and Biological Evaluations of 3-Substituted

Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular

Receptor Tyrosine Kinases

AUTHOR(S): Sun, Li; Tran, Ngoc; Tang, Flora; App, Harald; Hirth,

Peter; McMahon, Gerald; Tang, Cho

CORPORATE SOURCE: SUGEN Inc, Redwood City, CA, 94063, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(14),

2588-2603

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

3-Substituted indolin-2-ones have been designed and synthesized as a novel class of tyrosine kinase inhibitors which exhibit selectivity toward different receptor tyrosine kinases (RTKs). These compds. have been evaluated for their relative inhibitory properties against a panel of RTKs in intact cells. By modifying the 3-substituted indolin-2-ones, we have identified compds. which showed selective inhibition of the ligand-dependent autophosphorylation of various RTKs at submicromolar levels in cells. Structure-activity anal. for these compds. and their relative potency and selectivity to inhibit particular RTKs has detd. that (1) 3-[(five-membered heteroaryl ring)methylidenyl]indolin-2-ones are highly specific against the VEGF (Flk-1) RTK activity, (2) 3-(substituted benzylidenyl)indolin-2-ones contg. bulky group(s) in the Ph ring at the C-3 position of indolin-2-ones showed high selectivity toward the EGF and Her-2 RTKs, and (3) the compd. contg. an extended side chain at the C-3 position of the indolin-2-one exhibited high potency and selectivity when tested against the PDGF and VEGF (Flk-1) RTKs. Recent published crystallog. data for two of these 3-substituted indolin-2-ones provides a rationale to suggest that these compds. may bind in the ATP binding pocket of RTKs. The structure-activity anal. supports the use of subsets of these compds. as specific chem. leads for the development of RTK-specific drugs with broad application for the treatment of human diseases.

194413-58-6P 210303-48-3P 210303-49-4P IT

210303-50-7P 210303-51-8P 210303-52-9P

210303-53-0P 210303-54-1P 210303-55-2P

210303-58-5P 210303-59-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and evaluation of 3-substituted indolin-2-ones as inhibitors of selective growth factor receptors)

RN 194413-58-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (CA INDEX NAME) (3Z) - (9CI)

Double bond geometry as shown.

RN 210303-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 210303-49-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & \text{HO}_2C \\ & \text{H} \\ & \text{N} \\ & \text{Z} \\ & \text{H} \\ \end{array}$$

RN 210303-50-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 210303-51-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 210303-52-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-6-fluoro-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 210303-53-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} H & \text{Me} & \text{Et} \\ \hline \\ Z & N \\ H & H \end{array}$$

RN 210303-54-1 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN210303-55-2 CAPLUS

2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-CNdihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

210303-58-5 CAPLUS RN

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4methyl-, (3Z)- (9CI) (CA INDEX NAME)

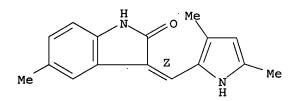
Double bond geometry as shown.

$$\begin{array}{c|c} H & Me \\ \hline \\ N & C \\ \hline \\ Me \\ Me \\ \end{array}$$

RN210303-59-6 CAPLUS

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-CN methyl-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT:

20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 115 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:151222 CAPLUS

DOCUMENT NUMBER:

128:164361

TITLE: INVENTOR(S): Crystal structures of a protein tyrosine kinase

Mohammadi, Moosa; Li, Sun; Liang, Congxin; Schlessinger, Joseph; Hubbard, Stevan R.; McMahon,

Gerald; Tang, Peng C.

PATENT ASSIGNEE(S):

Sugen, Inc., USA; Mohammadi, Moosa; Li, Sun; Liang,

Congxin; Schlessinger, Joseph; Hubbard, Stevan R.;

McMahon, Gerald; Tang, Peng C.

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SOURCE:
                         PCT Int. Appl., 493 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                           APPLICATION NO.
     PATENT NO.
                     KIND DATE
                                           WO 1997-US14885 19970821
     WO 9807835
                      A2
                            19980226
     WO 9807835
                      Α3
                           19981001
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            DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
            PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
            UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
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     AU 9741603
                            19980306
                                           AU 1997-41603
                      A1
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     EP 931152
                            19990728
                                           EP 1997-939534
                      A2
                                                            19970821
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                      T2
                            20010911
                                           JP 1998-511036
     JP 2001514484
                                                            19970821
PRIORITY APPLN. INFO.:
                                        US 1996-701191
                                                           19960821
                                                       А
                                        US 1996-34168P
                                                         Р
                                                            19961219
                                        WO 1997-US14885 W 19970821
OTHER SOURCE(S):
                        MARPAT 128:164361
     The present invention relates to the 3-dimensional structures of a protein
     tyrosine kinase optionally complexed with one or more compds. Thus, a
     310-amino acid fragment fibroblast growth factor receptor 1 (residues
     456-765, FGFR1) was recombinantly prepd. contg. the amino acid
     substitutions Cys488.fwdarw.Ala, Cys584.fwdarw.Ser, and Leu457.fwdarw.Val,
     and an addnl. 5 residues (Ser-Ala-Ala-Gly-Thr) at the N-terminus. X-ray
     crystallog. yielded the at. structural coordinates of cryst. FGFR1 and its
     complexes with adenylyl diphosphonate, 3-[(3-(2-carboxyethyl)-4-
     methylpyrrol-5-yl)methylene]-2-indolinone, or 3-[4-(4-formylpiperazine-1-
    yl)benzylidenyl]-2-indolinone. Two forms of cryst. FGFR1 were obtained:
     one form (designated C2-A form) with unit cell dimensions of a = 208.3, b
     = 57.2, c = 65.5.ANG. and .beta. = 107.2.degree., and another C2-B form
     with dimensions a = 211.6, b = 51.3, c = 66.1.ANG. and .beta. =
     107.7.degree.. The overall structure of FGFR1 is bi-lobate.
     N-terminal lobe of FGFR1 spans amino acid residues 456-567 and comprises a
     curled .beta.-sheet of five antiparallel strands and one .alpha.-helix.
     The C-terminal lobe spans amino acid residues 568-765 and comprises two
     .beta.-strands and seven .alpha.-helixes. The at. coordinates that define
     the structures of the protein tyrosine kinase and any of the compds. bound
     to it are pertinent to methods for detg. the 3-dimensional structures of
     protein tyrosine kinases with unknown structure and to methods that
     identify modulators of protein tyrosine kinase functions.
ΙT
     186611-14-3D, complex with fibroblast growth factor receptor 1
    RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological
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(crystal structures of a protein tyrosine kinase)

ylidene) methyl] -4-methyl- (9CI) (CA INDEX NAME)

1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-

Page 19

RN

CN

study); USES (Uses)

186611-14-3 · CAPLUS

$$^{\rm H}_{
m N}$$
  $^{\rm O}_{
m CH}$   $^{\rm H}_{
m N}$   $^{\rm CH}_{
m 2}$   $^{\rm CH}_{
m 2}$   $^{\rm CH}_{
m 2}$   $^{\rm CO}_{
m 2}$   $^{\rm H}$ 

L4 ANSWER 116 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:147306 CAPLUS

DOCUMENT NUMBER:

128:204803

TITLE:

Indolinone combinatorial libraries and related

products and methods for the treatment of disease

INVENTOR(S):

Tang, Peng Cho; Sun, Li; McMahon, Gerald; Hirth, Klaus

Peter; Shawver, Laura Kay; et al.

PATENT ASSIGNEE(S):

Sugen, Inc., USA; Tang, Peng Cho; Sun, Li; McMahon,

Gerald

SOURCE:

PCT Int. Appl., 293 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

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					A1 19980226							36	19970820						
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					A1 19990721														
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	JP 2001503736			T2 20010321			0321		Ċ	JP 19	98-53	3	19970820						
	ΕP	12478	303		A2		20021009			I	EP 20	02-7	7564		19970	820			
	ΕP	P 1247803			A3		20021016												
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									τ	JS :	L996-	31589	5 P	P	19961	L205			
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									τ	JS 1	L996-	31588	3P	P	19961	L205			
									ζ	JS 1	1996-	32546	5 P	P	19961	L205			
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									ζ	JS 1	L997-	45714	1 P	P	19970	505			

US 1997-45715P 19970505 19970505 US 1997-46843P Р US 1996-45715P P 19961205 US 1997-31565P 19970505 EP 1997-939480 A3 19970820 US 1997-915366 A3 19970820 WO 1997-US14736 W 19970820

OTHER SOURCE(S):

MARPAT 128:204803

Ι

GI

The invention relates to indolinone derivs. capable of modulating, AB regulating, and/or inhibiting protein kinase signal transduction. compds. are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK protein kinase can be obtained by adding chem. substituents to the 3-[(indole-3yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. Indolinone compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosol. indolinone compds. that are tyrosine kinase inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepd. by combinatorial condensation of certain (un) substituted indolinones with aldehydes at the 3-position. complete inhibition of MET kinase at chimeric MET receptors in vitro. IT 203989-05-3P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5yl]methylidenyl]-5,7-dibromo-2-indolinone 203989-08-6P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl)ethyl]-4-[(ethoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5,7-dibromo-2-indolinone 203989-10-0P, 3-[[2,3-Bis(methoxycarbonyl)-5-methylpyrrol-4yl]methylidenyl]-5,7-dibromo-2-indolinone 203989-14-4P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-iodo-2indolinone 203989-17-7P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl) ethyl] -4-[(ethoxycarbonyl) methyl]pyrrol-5-yl]methylidenyl]-5-iodo-2-indolinone 203989-19-9P, 3-[[2,3-Bis(methoxycarbonyl)-5methylpyrrol-4-yl]methylidenyl]-5-iodo-2-indolinone 203989-24-6P , 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-bromo-4methyl-2-indolinone 203989-27-9P, 3-[[2-(Ethoxycarbonyl)-3-[2-(ethoxycarbonyl) ethyl] -4 - [(ethoxycarbonyl) methyl] pyrrol -5 -yl] methylidenyl] -5-bromo-4-methyl-2-indolinone 203989-29-1P, 3-[[2,3-

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Bis (methoxycarbonyl) -5-methylpyrrol-4-yl]methylidenyl] -5-bromo-4-methyl-2-
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5-[(methylamino)sulfonyl]-2-indolinone 203989-43-9P,
3-[[2,3-Bis(methoxycarbonyl)-5-methylpyrrol-4-yl]methylidenyl]-5-
[(methylamino) sulfonyl]-2-indolinone 203989-52-0P,
3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-yl]methylidenyl]-5-[[[4-
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203989-75-7P, 3-[[2,4-Dimethyl-3-(ethoxycarbonyl)pyrrol-5-
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203991-82-6P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-bromo-4-
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[(methoxycarbonyl)methyl]pyrrol-5-yl]methylidenyl]-5-[[[4-
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(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203995-78-2P
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(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203995-84-0P
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yl) methylidenyl] -5-(2-chloroethyl) -2-indolinone 203996-03-6P,
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3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
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indolinone 203996-53-6P; 3-[(2,4-Diethylpyrrol-5-
y1) methylideny1]-5-(morpholinosulfony1)-2-indolinone 203996-63-8P
  3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
204003-90-7P 204003-91-8P 204003-96-3P
204003-97-4P 204004-86-4P 204004-92-2P
204004-94-4P 204005-03-8P 204005-21-0P
204005-38-9P 204005-39-0P 204005-46-9P
204005-54-9P 204005-56-1P 204005-58-3P
204005-59-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (prepn. and testing of indolinone combinatorial library as protein
   kinase inhibitors)
203989-05-3 CAPLUS
1H-Pyrrole-3-carboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-
ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)
```

RN CN

RN 203989-08-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-10-0 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

RN 203989-14-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline N & CH & N & Me \\ \hline Me & C - OEt \\ \hline \parallel & O \\ \end{array}$$

RN 203989-17-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-19-9 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & &$$

RN 203989-24-6 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-27-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-29-1 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

RN 203989-35-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-40-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-43-9 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 203989-52-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-56-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-58-6 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

RN 203989-65-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & H & O & H & Me \\ \hline O & & & & Me & C-OEt \\ \hline O & & & & & O \\ \hline \end{array}$$

RN 203989-68-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-70-2 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 203989-75-7 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 203989-78-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{C1CH}_2-\text{CH}_2 & & & \\ & &$$

RN 203989-80-4 CAPLUS

CN 1H-Pyrrole-2,3-dicarboxylic acid, 4-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-5-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & MeO-C & O \\ H & N & O & MeO-C & O \\ \hline CH & CH & N \\ Me & Me & H \end{array}$$

RN 203989-88-2 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ Br & & \\ & & \\ Br & & \\ & &$$

RN 203989-98-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203990-08-3 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203990-18-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203990-28-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203990-38-9 CAPLUS

CN Morpholine, 4-[[3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203990-48-1 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 $H$ 
 $CH$ 
 $H$ 
 $N$ 
 $Me$ 
 $Et$ 

RN 203991-62-2 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 203991-72-4 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203991-82-6 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203991-92-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H & Me \\
 & MeNH-S & & Me & Me
\end{array}$$

RN 203992-02-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203992-12-5 CAPLUS

CN Morpholine, 4-[[3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203992-22-7 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 $H$ 
 $N$ 
 $CH$ 
 $N$ 
 $Me$ 

RN 203994-35-8 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 203994-53-0 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & CH_2-C-OMe \\ \hline & O & CH_2-C-OMe \\ \end{array}$$

RN 203994-72-3 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-2-chloro-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203994-91-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & H & O \\
 & H & C1 \\
 & CH & C1
 & O \\
 & O & CH_2-C-OMe
\end{array}$$

RN 203995-11-3 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-26-0 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-36-2 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 203995-39-5 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5,7-dibromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ Br & & \\$$

RN 203995-42-0 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 203995-48-6 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-51-1 CAPLUS

CN 2H-Indol-2-one, 3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-1,3-dihydro-5-iodo- (9CI) (CA INDEX NAME)

RN 203995-57-7 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[(5-bromo-1,2-dihydro-4-methyl-2-oxo-

3H-indol-3-ylidene)methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H & O \\ & H & C & H & C \\ & CH & N & C \\ & Me & MeO-C & Me \\ & & O \\ & & O \\ \end{array}$$

RN 203995-60-2 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 203995-66-8 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-[(methylamino)sulfonyl]-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H & O \\
 & MeNH-S & C-OEt \\
 & O & MeO-C & Me
\end{array}$$

RN 203995-69-1 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203995-75-9 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-2-oxo-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} F_3C \\ \hline \\ NH-S \\ \hline \\ O \\ \hline \\ NH-C-OEt \\ \hline \\ MeO-C \\ \hline \\ Me \\ O \\ \end{array}$$

RN 203995-78-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203995-84-0 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[1,2-dihydro-5-(4-morpholinylsulfonyl)-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

RN 203995-87-3 CAPLUS

CN Morpholine, 4-[[3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203995-93-1 CAPLUS

CN 1H-Pyrrole-2,4-dicarboxylic acid, 5-[[5-(2-chloroethyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-3-methyl-, 2-ethyl 4-methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 203995-96-4 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(1,4-dimethyl-1H-pyrrol-3-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1CH_2-CH_2$$
 $H$ 
 $CH$ 
 $CH$ 
 $CH$ 
 $CH$ 
 $Me$ 

RN 203996-03-6 CAPLUS

CN 2H-Indol-2-one, 5,7-dibromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 203996-13-8 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-iodo-(9CI) (CA INDEX NAME)

RN 203996-23-0 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H \\ \hline & N & CH & N \\ \hline & & Et \\ \end{array}$$

RN 203996-33-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 203996-43-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

RN 203996-53-6 CAPLUS

CN Morpholine, 4-[[3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 203996-63-8 CAPLUS

CN 2H-Indol-2-one, 5-(2-chloroethyl)-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O \\ & & H \\ & CH \\ & & CH \\ & & Et \\ \end{array}$$

RN 204003-90-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-91-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-96-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[[3,5-bis(1-methylethyl)-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 204003-97-4 CAPLUS

CN 1H-Indole-5-propanoic acid, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)

$$H_{N} = 0$$
 $H_{N} = 0$ 
 $H_{N$ 

RN 204004-86-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-amino-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$H_2N$$
 $H_2N$ 
 $H_2N$ 

RN 204004-92-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 204004-94-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-4-methyl-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline \\ Me & CH_2-CH_2-C-OMe \end{array}$$

RN 204005-03-8 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & \\ \hline & CH & \\ \hline & Me & CH_2-CH_2-C-OMe \end{array}$$

RN 204005-21-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1,2,4-trimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 204005-38-9 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ N & CH & N \end{array}$$
 Me

RN 204005-39-0 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2N}$$
 $CH$ 
 $Me$ 
 $Me$ 

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-54-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-methyl- (9CI) (CA INDEX NAME)

RN 204005-56-1 CAPLUS

CN 2H-Indol-2-one, 5-amino-3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 204005-58-3 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

204005-59-4 CAPLUS RN

2H-Indol-2-one, 3-[(3,5-diethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-CN methyl- (9CI) (CA INDEX NAME)

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 15

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 117 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:640690 CAPLUS

DOCUMENT NUMBER:

127:314804

TITLE:

Assays for KDR/FLK-1 receptor tyrosine kinase

inhibitors, and use of the inhibitors for treatment of

vasculogenesis- and angiogenesis-related diseases Hirth, Klaus P.; McMahon, Gerald; Shawver, Laura K.

INVENTOR(S): PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 65 pp.

CODEN: PIXXD2 ·

DOCUMENT TYPE:

Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	KIND DATE			A.	PPLI	CATIO	o. 1	DATE										
									-									
WO	WO 9734920			A:	A1 19970925			WO 1997-US3378 19970304										
	W:	AL,	AM,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CU,	CZ,	EE,	GE,	GH,	
		HU,	IL,	IS,	JP,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LT,	LV,	MD,	MG,	MK,	
		MN,	MX,	NO,	NZ,	PL,	RO,	RU,	SG,	SI,	SK,	TJ,	TM,	TR,	TT,	UA,	UZ,	
		VN,	YU,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM			•			
	RW:	GH,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	
		GR,	ΙE,	IT,	LU,	MC,	NL;	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	
		ML,	MR,	ΝE,	SN,	TD,	TG											
AU	A1 19971010				AU 1997-20667						19970304							
PRIORITY	. :				US 1996-621734						19960321							
				•				1	WO 1	997-1	JS33′	78		1997	0304			

AB Processes are disclosed for the identification of compds. and pharmaceutical compns. capable of selectively and potently inhibiting KDR/FLK-1 tyrosine kinase signal transduction in order to inhibit vasculogenesis and/or angiogenesis. The invention also relates to compds. and compns. identified using the methods of the invention and the use

thereof for the treatment of disease relating to inappropriate vasculogenesis and/or angiogenesis. The invention provides an assay cascade comprised of several "filter steps" of increasing selectivity which identify a limited subset of candidate compds. affecting the VEGF receptor on the mol. level.

IT 204005-46-9, SU 5416

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(KDR/FLK-1 receptor tyrosine kinase inhibitor identification assay, and use of compds. for treatment of vasculogenesis- and angiogenesis-related diseases)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

ANSWER 118 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1997:322412 CAPLUS

DOCUMENT NUMBER:

127:44439

TITLE:

Structure of the tyrosine kinase domain of fibroblast growth factor receptor in complex with inhibitors

AUTHOR (S):

Mohammadi, Moosa; McMahon, Gerald; Sun, Li; Tang, Cho;

Hirth, Peter; Yeh, Brian K.; Hubbard, Stevan R.; Schlessinger, Joseph

CORPORATE SOURCE:

Dep. Pharmacology, New York Univ. Med. Center, New

York, NY, 10016, USA

SOURCE:

Science (Washington, D. C.) (1997), 276(5314), 955-960

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER:

American Association for the Advancement of Science

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB A new class of protein tyrosine kinase inhibitors was identified that is based on an oxindole core (indolinones). Two compds. from this class inhibited the kinase activity of fibroblast growth factor receptor 1 (FGFR1) and showed differential specificity toward others receptor tyrosine kinases. Crystal structures of the tyrosine kinase domain of FGFR1 in complex with the two compds. were detd. The oxindole occupies the sites in which the adenine of ATP binds, whereas the moieties that extend from the oxindole contact residues in the hinge region between the two kinase lobes. The more specific inhibitor of FGFR1 induces a conformational change in the nucleotide-binding loop. This structural information will facilitate the design of new inhibitors for use in the treatment of cancer and other diseases in which cell signaling by tyrosine kinases plays a crucial role in disease pathogenesis.

IT 186611-14-3, SU 5402

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(inhibitor; structure of tyrosine kinase domain of fibroblast growth

factor receptor in complex with inhibitors)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline \\ CH & N \\ \hline \\ Me & CH_2-CH_2-CO_2H \\ \end{array}$$

L4 ANSWER 119 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1997:140244 CAPLUS

DOCUMENT NUMBER:

126:139901

TITLE:

Indolinone compounds capable of modulating tyrosine

kinase signal transduction

INVENTOR(S):

Tang, Peng Cho; Sun, Li; Mcmahon, Gerald

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English ·

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PA'	TENT	NO.		KI	ND	DATE			Al									
						<del>-</del>												
WO	9640	116		A1 19961219					W	19	96-U	3	19960605					
	W:	AL,	AM,	AU,	ΑZ,	BB,	BG,	BR,	BY,	CA,	CN,	CZ,	EE,	FI,	GE,	HU,	IL,	
		IS,	JΡ,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,	LT,	LV,	MD,	MG,	MK,	MN,	MX,	
		NO,	NZ,	PL,	RO,	RU,	SG,	SI,	SK,	TJ,	TM,	TR,	TT,	UΑ,	UZ,	VN,	AM,	
		AZ,	BY					•										
	RW:	ΚE,	LS,	MW,	SD,	SZ,	ŪĠ,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	
														CM,				
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ΕP	7699	47		В	1	2001	0502											
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		PT,	SE															
BR	9606	410		Α		1997	1230		В	R 19	96-64	410		19960	0605			
JР	1050	4323		T2 19980428					JI	P 19:	96-50	0136	3	19960	0605			
ΕP	9349	31		A	2	1999	0811		El	P 19:	99-10	0366	7	19960	0605			
EP	9349	31		Α	3	1999	1020											
	R:	AT,	BE,	CH,	DE,	DK;	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
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JP	2000	0264	12	A	2	2000	0125		JI	2 19:	99-1	5956	7	19960	0605			
ΑT	2008	63		E		2001	0515		A.	Г 19	96-9:	1809	3	19960	0605			
														19960	0605			
	3231													19960				
														1996				

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HK 1011933
                      A1
                            20020118
                                           HK 1998-113193
                                                            19981211
     US 2002022626
                       A1
                            20020221
                                           US 2000-617529
                                                            20000713
                                                        A 199506.07
PRIORITY APPLN. INFO.:
                                        US 1995-485323
                                        EP 1996-918093
                                                         A3 19960605
                                        JP 1997-501363
                                                         A3 19960605
                                        WO 1996-US8903
                                                         W 19960605
                                        US 1997-915366
                                                         A3 19970820
OTHER SOURCE(S):
                         MARPAT 126:139901
     The present invention relates to org. mols. capable of modulating tyrosine
     kinase signal transduction in order to regulate, modulate and/or inhibit
     abnormal cell proliferation. Representatives of the 5 different classes
     of compds. described are SU 4932 [3-(2-chloro-4-hydroxybenzylidenyl)-2-
     indolinone], SU 4312 [3-(4-dimethylaminobenzylidenyl)-2-indolinone], SU
     5416 {3-[(2,4-dimethylpyrrol-5-yl)methylene]-2-indolinone}, SU 5204
     [3-(2-ethoxybenzylidenyl)-2-indolinone], and SU 4942 [3-(4-
     bromobenzylidenyl)-2-indolinone]. Diseases which these compds. and their
     pharmaceutically acceptable prepns. may be effective against include
     arthritis, hepatic cirrhosis, diabetic nephropathy and psoriasis.
IT
     15966-93-5P, SU 5408 186610-94-6P, SU 5406
     186611-14-3P, SU 5402 186611-16-5P, SU 5405
     186611-17-6P, SU 5407 186611-29-0P, SU 5453
     186611-30-3P, SU 5454 186611-31-4P, SU 5455 186611-
     33-6P, SU 5459 186611-34-7P, SU 5460 186611-37-0P
     , SU 5463 186611-39-2P, SU 5465 186611-48-3P, SU 5477
     186611-50-7P, SU 5479 186611-56-3P, SU 5614
     186611-67-6P, SU 5626 204005-46-9P, SU 5416
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of indolinones capable of modulating tyrosine kinase signal
        transduction)
RN
     15966-93-5 CAPLUS
     1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-
CN
     ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)
```

RN 186610-94-6 CAPLUS CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
  $^{\rm CH}$   $^{\rm CH}$ 

RN 186611-16-5 CAPLUS

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & CH & N \\ \hline & O & CH & N \\ \hline & MeO-C-CH_2-CH_2 & Me \\ \end{array}$$

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-30-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl- (9CI) (CA INDEX NAME)

RN 186611-33-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 186611-34-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-39-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-50-7 CAPLUS

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline N & CH & Me \\ \hline \\ Me & C-Me \\ \| \\ CH_2 \\ \end{array}$$

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-67-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

4 ANSWER 120 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1968:496372 CAPLUS

DOCUMENT NUMBER: 69:96372

TITLE: Stokvis reaction. XVII. Vilsmeier reaction with

pyrrole and pyrrolone derivatives

Schnierle, Franz; Reinhard, Horst; Dieter, Norbert; AUTHOR (S):

Lippacher, Eberhard; Von Dobeneck, Henning

Tech. Hochsch. Muenchen, Munich, Fed. Rep. Ger. CORPORATE SOURCE:

SOURCE: Justus Liebigs Annalen der Chemie (1968), 715, 90-7

CODEN: JLACBF; ISSN: 0075-4617

DOCUMENT TYPE: Journal LANGUAGE: German

Vilsmeier formylation of 4-methyl-3-acetyl-2-methoxycarbonylpyrrole gave

4-methyl-2-methoxycarbonyl-3-(1-chloro-3-dimethylimmonio-1-

propenyl)pyrrole perchlorate. Formylation of I (R = Me or Et) in the presence of POX3 (X = Br or Cl) gave II. 3-methyl-4-(R-substituted) 3-pyrrolin-2-one, treated as above, gave 3-methyl-4-(R-substituted)-5-(X-

substituted) - 2 - formylpyrrole. The Vilsmeier reaction of

4-methyl-3-(R-substituted)-3-pyrrolin-2-one with ClCOCOCl gave III. references.

19713-94-1P IT

> RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN 19713-94-1 CAPLUS

2-Indolinone, 3-[(5-chloro-3,4-dimethylpyrrol-2-yl)methylene]- (8CI) CN INDEX NAME)

ANSWER 121 OF 121 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1967:433817 CAPLUS

DOCUMENT NUMBER: 67:33817

Isoindigo dyes of the pyrrole series TITLE:

AUTHOR (S):

Treibs, Alfred; Jacob, Karl; Dietl, Anton Tech. Hochsch. Munich, Munich, Fed. Rep. Ger. CORPORATE SOURCE: Justus Liebigs Ann. Chem. (1967), 702, 112-30 SOURCE:

DOCUMENT TYPE: Journal LANGUAGE: German

For diagram(s), see printed CA Issue.

AB The dye obtained by lactam ring closure of PhCOCH2CH2CO2H (I) has the structure (II) of a phenylpyrrole-isoindigo (P-II) proposed by Kugel, and is identical with the compd. obtained from the O analog, the Pechmann dye In addn. to P-II, 4-(3-carboxy-1-phenylpropylidene)-2-phenyl-2pyrrolin-5-one is formed by condensation of 2-phenyl-2-pyrrolin-5-one with

I, which can also be converted into P-II via a readily proceeding retrocrotonization-retroaldol reaction. New methods for the synthesis of pyrrole-indole-isoindigo derivs. (e.g. IV, X = O, NH, and NMe) are

described. The pyrrolylpyrrolinones V (R = CO2Et) (VI) and V (R = H) (VII) and the pyrrolylpyrrole-isoindigo derivs. VIII (R = CO2Et) (IX) and VIII (R = H) (X) prepd. from VI and VII were obtained; IX and X are

derivs. of an .alpha., .beta., .alpha.-linked tetrapyrrole.

IT 15966-93-5P

> RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

RN 15966-93-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

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                BLAST(R) searching in REGISTRY available in STN on the Web
                FSTA has been reloaded and moves to weekly updates
NEWS 3 Jan 29
NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update
                frequency
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6 Mar 08 Gene Names now available in BIOSIS
     7 Mar 22
                TOXLIT no longer available
NEWS
NEWS 8 Mar 22
                TRCTHERMO no longer available
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAplus
                and USPATFULL
NEWS 10 Mar 28
                LIPINSKI/CALC added for property searching in REGISTRY
                PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 11 Apr 02
NEWS 12 Apr 08
                "Ask CAS" for self-help around the clock
                BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 13 Apr 09
NEWS 14 Apr 09
                ZDB will be removed from STN
                US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 15 Apr 19
                Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 16 Apr 22
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 19 Jun 03 New e-mail delivery for search results now available
NEWS 20 Jun 10 MEDLINE Reload
NEWS 21 Jun 10 PCTFULL has been reloaded
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NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002

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Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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Uploading 09897755.str

L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

T.1 STR

G1 0, S

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=> s 11 sss sam
SAMPLE SEARCH INITIATED 16:31:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 633 TO ITERATE

100.0% PROCESSED 633 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

50 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 11151 TO 14169 PROJECTED ANSWERS: 2635 TO 4203

L2 50 SEA SSS SAM L1

=> sl 1 full

SL IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> s l1 full

FULL SEARCH INITIATED 16:31:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 13065 TO ITERATE

100.0% PROCESSED 13065 ITERATIONS

3510 ANSWERS

SEARCH TIME: 00.00.03

L3 3510 SEA SSS FUL L1

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ENTRY SESSION 140.66 140.87

FULL ESTIMATED COST

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=> s 13 full

L4 390 L3

=> s 14 and tyrosine?

115982 TYROSINE?

L5 66 L4 AND TYROSINE?

=> d 15 56-66 ibib abs hitstr

L5 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:322412 CAPLUS

DOCUMENT NUMBER: 127:44439

TITLE: Structure of the tyrosine kinase domain of

fibroblast growth factor receptor in complex with

inhibitors

AUTHOR(S): Mohammadi, Moosa; McMahon, Gerald; Sun, Li; Tang, Cho;

Hirth, Peter; Yeh, Brian K.; Hubbard, Stevan R.;

Schlessinger, Joseph

CORPORATE SOURCE: Dep. Pharmacology, New York Univ. Med. Center, New

York, NY, 10016, USA

SOURCE: Science (Washington, D. C.) (1997), 276(5314), 955-960

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal LANGUAGE: English

AB A new class of protein **tyrosine** kinase inhibitors was identified that is based on an oxindole core (indolinones). Two compds. from this class inhibited the kinase activity of fibroblast growth factor receptor 1 (FGFR1) and showed differential specificity toward others receptor

tyrosine kinases. Crystal structures of the tyrosine

kinase domain of FGFR1 in complex with the two compds. were detd. The oxindole occupies the sites in which the adenine of ATP binds, whereas the moieties that extend from the oxindole contact residues in the hinge region between the two kinase lobes. The more specific inhibitor of FGFR1 induces a conformational change in the nucleotide-binding loop. This structural information will facilitate the design of new inhibitors for use in the treatment of cancer and other diseases in which cell signaling by tyrosine kinases plays a crucial role in disease pathogenesis.

IT 186611-14-3, SU 5402

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(inhibitor; structure of **tyrosine** kinase domain of fibroblast growth factor receptor in complex with inhibitors)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

L5 ANSWER 57 OF 66 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1997:140244 CAPLUS

DOCUMENT NUMBER: 126:139901

TITLE: Indolinone compounds capable of modulating

tyrosine kinase signal transduction

```
Tang, Peng Cho; Sun, Li; Mcmahon, Gerald
INVENTOR(S):
                         Sugen, Inc., USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 133 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                     KIND DATE
                                         APPLICATION NO. DATE
     PATENT NO.
     WO 9640116
                     A1
                           19961219
                                         WO 1996-US8903 19960605
         W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IL,
             IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX,
             NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM,
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
            MR, NE, SN, TD, TG
                           19990309
                                          US 1995-485323
                      Α
                                                            19950607
     US 5880141
                                          CA 1996-2192797 19960605
                            19961219
     CA 2192797
                      AA
     AU 9660441
                            19961230
                                          AU 1996-60441
                                                            19960605
                      Α1
     AU 706597
                      В2
                            19990617
                                          EP 1996-918093
     EP 769947
                      Α1
                            19970502
                                                            19960605
     EP 769947
                            20010502
                      В1
           AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL,
             PT, SE
     BR 9606410
                           19971230
                                           BR 1996-6410
                                                            19960605
                      Α
                      Т2
                           19980428
                                           JP 1996-501363
                                                            19960605
     JP 10504323
     EP 934931
                      A2
                           19990811
                                          EP 1999-103667
                                                            19960605
                           19991020
     EP 934931
                      A3
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI
                                          JP 1999-159567
     JP 2000026412
                      A2
                            20000125
                                                            19960605
     AT 200863
                            20010515
                                          AT 1996-918093
                                                            19960605
                      E
                                          ES 1996-918093
     ES 2159741
                      Т3
                           20011016
                                                            19960605
                      B2
                           20011119
                                          JP 1997-501363
                                                            19960605
     JP 3231044
     NO 9605377
                                          NO 1996-5377
                           19970212
                                                            19961213
                      Α
PRIORITY APPLN. INFO.:
                                       US 1995-485323
                                                        A 19950607
                                                        A3 19960605
                                        EP 1996-918093
                                                        A3 19960605
                                        JP 1997-501363
                                                        W 19960605
                                        WO 1996-US8903
OTHER SOURCE(S):
                        MARPAT 126:139901
AB
     The present invention relates to org. mols. capable of modulating
     tyrosine kinase signal transduction in order to regulate, modulate
     and/or inhibit abnormal cell proliferation. Representatives of the 5
     different classes of compds. described are SU 4932 [3-(2-chloro-4-
     hydroxybenzylidenyl)-2-indolinone], SU 4312 [3-(4-
     dimethylaminobenzylidenyl)-2-indolinone], SU 5416 {3-[(2,4-dimethylpyrrol-
     5-yl)methylene]-2-indolinone, SU 5204 [3-(2-ethoxybenzylidenyl)-2-
     indolinone], and SU 4942 [3-(4-bromobenzylidenyl)-2-indolinone]. Diseases
     which these compds. and their pharmaceutically acceptable prepns. may be
     effective against include arthritis, hepatic cirrhosis, diabetic
     nephropathy and psoriasis.
     2731-46-6P, SU 5432 3367-90-6P, SU 5212
ΙT
     15966-93-5P, SU 5408 62540-08-3P, SU 5208
     64259-01-4P, SU 4798 64259-03-6P, SU 5438
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64259-04-7P, SU 5409 64259-05-8P, SU 5430 91822-51-4P, SU 4314 186610-92-4P, SU 5401 186610-93-5P, SU 5404 186610-94-6P, SU 5406

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186610-96-8P, SU 5419 186610-97-9P, SU 5424
186610-98-0P, SU 5427 186611-12-1P, SU 5217
186611-14-3P, SU 5402 186611-15-4P, SU 5403
186611-16-5P, SU 5405 186611-17-6P, SU 5407
186611-18-7P, SU 5410 186611-19-8P, SU 5418
186611-20-1P, SU 5420 186611-21-2P, SU 5421
186611-22-3P, SU 5422 186611-23-4P, SU 5423
186611-24-5P, SU 5425 186611-25-6P, SU 5426
186611-26-7P, SU 5428 186611-27-8P, SU 5431
186611-28-9P, SU 5451 186611-29-0P, SU 5453
186611-30-3P, SU 5454 186611-31-4P, SU 5455
186611-32-5P, SU 5456 186611-33-6P, SU 5459
186611-34-7P, SU 5460 186611-35-8P, SU 5461
186611-36-9P, SU 5462 186611-37-0P, SU 5463
186611-38-1P, SU 5464 186611-39-2P, SU 5465
186611-41-6P, SU 5468 186611-42-7P, SU 5469
186611-43-8P, SU 5472 186611-44-9P, SU 5473
186611-45-0P, SU 5474 186611-46-1P, SU 5475
186611-47-2P, SU 5476 186611-48-3P, SU 5477
186611-49-4P, SU 5478 186611-50-7P, SU 5479
186611-53-0P, SU 5612 186611-54-1P, SU 5613
186611-56-3P, SU 5614 186611-57-4P, SU 5615
186611-58-5P, SU 5616 186611-59-6P, SU 5617
186611-60-9P, SU 5618 186611-61-0P, SU 5619
186611-62-1P, SU 5620 186611-63-2P, SU 5621
186611-65-4P, SU 5624 186611-66-5P, SU 5625
186611-67-6P, SU 5626 186611-68-7P, SU 5627
186611-69-8P, SU 5628 186611-71-2P, SU 5629
186611-73-4P, SU 5630 186611-75-6P, SU 5631
186611-77-8P, SU 5632 186611-78-9P, SU 5633
186611-79-0P, CS 7127 186611-80-3P, CS 7128
186611-81-4P, CS 7129 186611-82-5P, CS 7130
186611-83-6P, CS 7131 186611-84-7P, CS 7132
186611-85-8P, CS 7133 186611-86-9P, CS 7135
186611-87-0P, CS 7136 186611-88-1P, CS 7137
186611-89-2P, CS 7138 186611-90-5P, CS 7139
186611-91-6P, CS 7140 186611-92-7P, CS 7141
186611-93-8P, CS 7142 186611-94-9P, CS 7143
186611-95-0P, CS 7144 186611-96-1P, CS 7145
186611-97-2P, CS 7146 186611-98-3P, CS 7147
204005-46-9P, SU 5416
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (prepn. of indolinones capable of modulating tyrosine kinase
   signal transduction)
2731-46-6 CAPLUS
2H-Indol-2-one, 1,3-dihydro-3-[(5-nitro-2-furanyl)methylene]- (9CI) (CA
INDEX NAME)
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RN

CN

RN 3367-90-6 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-(4-pyridinylmethylene)- (9CI) (CA INDEX NAME)

RN 15966-93-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 62540-08-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-thienylmethylene)- (9CI) (CA INDEX NAME)

RN 64259-01-4 CAPLUS

CN 2H-Indol-2-one, 3-(2-furanylmethylene)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 64259-03-6 CAPLUS

CN 2H-Indol-2-one, 3-[(5-bromo-2-furanyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 64259-04-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-iodo-2-furanyl)methylene]- (9CI) (CA INDEX NAME)

RN 64259-05-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-furanyl)methylene]- (9CI) (CA INDEX NAME)

RN 91822-51-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186610-92-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-methyl-2-thienyl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-93-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-94-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186610-96-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-(methylthio)-2-thienyl]methylene]- (9CI) (CA INDEX NAME)

RN 186610-97-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-thienyl)methylene]- (9CI) (CA INDEX NAME)

RN 186610-98-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-2-thienyl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-12-1 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3,5-bis(trifluoromethyl)phenyl]-2-furanyl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-14-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

$$^{\rm H}_{\rm N}$$
  $^{\rm O}$   $^{\rm H}_{\rm N}$   $^{\rm N}$   $^{\rm CH}_{\rm 2}-{\rm CH}_{\rm 2}-{\rm CO}_{\rm 2}{\rm H}$ 

RN 186611-15-4 CAPLUS

CN 2H-Indol-2-one, 3-[(3,4-dibromo-5-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-16-5 CAPLUS

CN 1H-Pyrrole-2-carboxaldehyde, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3,4-dimethyl- (9CI) (CA INDEX NAME)

RN 186611-17-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 186611-18-7 CAPLUS

CN 3-Furancarboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-19-8 CAPLUS

CN 2H-Indol-2-one, 3-[(3-bromo-2-thienyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-20-1 CAPLUS

CN 2H-Indol-2-one, 3-[(5-chloro-2-thienyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-21-2 CAPLUS

CN 2H-Indol-2-one, 3-[(4,5-dimethyl-2-furanyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-22-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-nitro-2-threnyl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-23-4 CAPLUS

CN 2-Thiophenecarboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

RN 186611-24-5 CAPLUS

CN 2H-Indol-2-one, 3-[(5-bromo-2-thienyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-25-6 CAPLUS

CN 2H-Indol-2-one, 3-[(4-bromo-2-thienyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-26-7 CAPLUS

CN 2-Furansulfonic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 186611-27-8 CAPLUS
CN 2H-Indol-2-one, 3-[(5-ethyl-2-furanyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-28-9 CAPLUS CN 2H-Indol-2-one, 3-[(5-ethyl-2-thienyl)methylene]-1,3-dihydro- (9CI) (CA

H O CH S Et

INDEX NAME)

RN 186611-29-0 CAPLUS

CN 2H-Indol-2-one, 3-[(3-ethyl-4,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-30-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-31-4 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-ethyl-3-methyl-(9CI) (CA INDEX NAME)

RN 186611-32-5 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-diiodo-4-methyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-33-6 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 2-chloro-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-(methoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & C1 \\ \hline & CH & CH_2-C-OMe \\ \hline & O & CH_2-C-OMe \\ \hline &$$

RN 186611-34-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 4-acetyl-5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-3-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-35-8 CAPLUS

CN 2H-Indol-2-one, 3-[[1-(3,5-dichlorophenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-36-9 CAPLUS

CN 2H-Indol-2-one, 3-[[1-(4-chlorophenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-37-0 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-38-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(1-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-39-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-5-(ethoxycarbonyl)-4-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 186611-41-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-methyl-1H-imidazol-2-yl)methylene]-(9CI) (CA INDEX NAME)

RN 186611-42-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-thiazolyl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-43-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-1H-pyrazol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-44-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-45-0 CAPLUS

CN 2H-Indol-2-one, 3-[(4-chloro-1H-pyrazol-3-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-46-1 CAPLUS

CN 2H-Indol-2-one, 3-[[4-bromo-1-[(4-chlorophenyl)methyl]-1H-pyrazol-5-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-47-2 CAPLUS

CN 2H-Indol-2-one, 3-[(4-chloro-1-methyl-1H-pyrazol-3-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[(4-ethyl-3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-49-4 CAPLUS

CN 2H-Indol-2-one, 3-[(5-ethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-50-7 CAPLUS

CN 2H-Indol-2-one, 3-[[3,5-dimethyl-4-(1-methylethenyl)-1H-pyrrol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & Me & C-Me \\ & \parallel & \\ & CH_2 & \end{array}$$

RN 186611-53-0 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(1H-pyrrol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-54-1 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 186611-56-3 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 186611-57-4 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-58-5 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(2-thienylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-59-6 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(3-methyl-2-thienyl)methylene]-(9CI) (CA INDEX NAME)

RN 186611-60-9 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[(5-methyl-2-thienyl)methylene]-(9CI) (CA INDEX NAME)

RN 186611-61-0 CAPLUS

CN 2H-Indol-2-one, 5-chloro-3-[(5-ethyl-2-thienyl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 186611-62-1 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-[[5-(methylthio)-2-thienyl]methylene]- (9CI) (CA INDEX NAME)

RN 186611-63-2 CAPLUS

CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(1H-imidazol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-65-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-(1H-pyrrol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-66-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-1H-pyrrol-2-yl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

$$O_2N$$
 $H$ 
 $O_1$ 
 $O_2$ 
 $O_3$ 
 $O_4$ 
 $O_4$ 
 $O_4$ 
 $O_5$ 
 $O_4$ 
 $O_5$ 
 $O_6$ 
 $O_6$ 

RN 186611-67-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-68-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-5-nitro- (9CI) (CA INDEX NAME)

RN 186611-69-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-(2-thienylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-71-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-methyl-2-thienyl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-73-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-thienyl)methylene]-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-75-6 CAPLUS

CN 2H-Indol-2-one, 3-[(5-ethyl-2-thienyl)methylene]-1,3-dihydro-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-77-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-(methylthio)-2-thienyl]methylene]-5-nitro-(9CI) (CA INDEX NAME)

RN 186611-78-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-2-ylmethylene)-5-nitro- (9CI) (CA INDEX NAME)

RN 186611-79-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-oxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-80-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-oxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-81-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(5-oxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-82-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-thiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-83-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-thiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-84-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(5-thiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-85-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-86-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrazol-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-87-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-88-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-isoxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-89-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-isoxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-90-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(5-isoxazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-91-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-isothiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-92-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-isothiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-93-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(5-isothiazolylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-94-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-1,2,3-triazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-95-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1,3,4-thiadiazol-2-ylmethylene)- (9CI) (CA INDEX NAME)

RN 186611-96-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-phenyl-1,2,4-oxadiazol-3-yl)methylene]-(9CI) (CA INDEX NAME)

RN 186611-97-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(3-phenyl-1,2,4-oxadiazol-5-yl)methylene]-(9CI) (CA INDEX NAME)

RN 186611-98-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-phenyl-1,2,5-oxadiazol-3-yl)methylene]-(9CI) (CA INDEX NAME)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

L5 ANSWER 58 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:746204 CAPLUS

DOCUMENT NUMBER: 126:18783

TITLE: Substituted indolylmethylene-oxindole analogs as

tyrosine kinase inhibitors

INVENTOR(S): Battistini, Carlo; Ballinari, Dario; Ermoli,

Antonella; Penco, Sergio; Vioglio, Sergio

PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9632380	A1	19961017	WO 1996-EP1165	19960314

W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 1996-907500 19960314 EP 764152 19970326 A1 FR, GB, IT, SE R: DE, ES, JP 1996-530667 19960314 Т2 JP 10501821 19980217 US 1996-750208 19961204 US 5849710 Α 19981215 19950407 PRIORITY APPLN. INFO .: GB 1995-7298 WO 1996-EP1165 19960314

OTHER SOURCE(S): MARPAT 126:18783

GΙ

Indol-3-ylmethylene-2-oxindole derivs. I and their pharmaceutically AΒ acceptable salts are disclosed [wherein 1 or 2 of R, R1, R2, and R3 = X(CH2) mNH2, X(CH2) mNR4R5, X(CH2) mNHR6, NHC(:NH) NH2, NHC(:NH) NR4R5, NHC(:NH)NHR6, N:CHNH2, N:CHNR4R5, N:CHNHR6, X(CH2)mCOR7, CORa, COR8, YCOY'R9, NHR6, NHR10 group; remaining groups within R and R1-R3 = H, halo, amino, OH, alkyl, alkoxy, CO2H, alkoxycarbonyl, alkanoyloxy, cyano, NR4R5; X = O, S, NH; m = 1-4; 1 of R4 and R5 = H or alkyl, and other = alkyl; or NR4R5 forms satd. monoheterocycle; R6 = alkanoyl, 1- to 3-residue (un) substituted peptidyl; R7 = OH, amino, alkoxy, NR4R5; Ra = amino terminus of 1- to 3-unit peptidyl; R8 = alkoxy, phenylalkoxy, (CH2)nNH2, (CH2) nNR4R5, (CH2) nNHR6; n = 1-2; Y, Y' = NH, O; R9 = Ph, alkyl, phenylalkyl; R10 = mono-, di- or trihydroxyalkyl]. I have tyrosine kinase inhibiting activity, and are useful as antiproliferative, antimetastatic, anticancer, antiatheromatous, anti-Alzheimer, and immunomodulating agents. For example, 2-indolinone reacted with BrCH2COBr and AlCl3 to give the 5-(2-bromoacetyl) deriv., which underwent amination with piperidine and then condensation with indole-3-carboxaldehyde, to give title compd. II (FCE 28484). In tests for inhibition of p45 v-abl kinase and K562 leukemia cells in vitro, II had IC50 of 0.78 and 4.82 .mu.M, resp.

IT 168464-17-3P 184021-39-4P 184021-56-5P 184021-79-2P 184021-85-0P 184021-97-4P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

168464-17-3 CAPLUS RN

2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-CN (9CI) (CA INDEX NAME)

$$H_2N$$
 $H_2N$ 
 $H_3$ 
 $H_4$ 
 $H_4$ 
 $H_4$ 
 $H_5$ 
 $H_6$ 
 $H_6$ 
 $H_6$ 
 $H_7$ 
 $H_8$ 
 $H_$ 

RN 184021-39-4 CAPLUS

CN Carbamic acid, [2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 184021-56-5 CAPLUS

CN 2H-Indol-2-one, 5-[[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]amino]-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{O} \\ \text{CH}_2 - \text{NH} \\ \end{array} \begin{array}{c} \text{H} \\ \text{N} \\ \text{CH} \\ \end{array} \begin{array}{c} \text{H} \\ \text{N} \\ \text{OMe} \\ \end{array}$$

RN 184021-79-2 CAPLUS

CN Carbamic acid, [3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & &$$

RN 184021-85-0 CAPLUS

CN Carbamic acid, [[3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]carbonimidoyl]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ Br & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 184021-97-4 CAPLUS

CN Carbamic acid, [2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-

1H-indol-6-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

### IT 184020-98-2P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindole analogs as **tyrosine** kinase inhibitors)

RN 184020-98-2 CAPLUS

CN Propanamide, 2-amino-N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

# IT 181223-99-4P 184020-79-9P 184020-86-8P 184020-93-7P 184021-06-5P 184021-15-6P 184021-23-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindole analogs as **tyrosine** kinase inhibitors)

RN 181223-99-4 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{OH} & & \\ & & \\ \text{HO-} & \text{CH}_2 - \text{CH-} & \text{CH}_2 - \text{NH} \end{array}$$

RN 184020-79-9 CAPLUS

CN Methanimidamide, N'-[2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & N = CH-NMe_2 \\ \hline \\ CH & N & H \end{array}$$

RN 184020-86-8 CAPLUS

CN Guanidine, [3-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 184020-93-7 CAPLUS

CN Propanamide, 2-amino-N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-6-yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 184021-06-5 CAPLUS

CN L-Alaninamide, L-.alpha.-glutamyl-N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 184021-15-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-5-(1-piperidinylacetyl)-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

## ● HCl

RN 184021-23-6 CAPLUS

CN 2H-Indol-2-one, 5-(aminoacetyl)-1,3-dihydro-3-(1H-indol-3-ylmethylene)-(9CI) (CA INDEX NAME)

$$H_2N-CH_2-C$$
 $CH$ 
 $CH$ 
 $CH$ 

IT 184020-69-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindoles as **tyrosine** kinase inhibitors)

RN 184020-69-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-5-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

L5 ANSWER 59 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:577724 CAPLUS

DOCUMENT NUMBER: 125:221574

TITLE: Preparation of hydrosoluble 3-arylidene-2-oxyindole

tyrosine kinase inhibitors

INVENTOR(S): Buzzetti, Franco; Brasca, Maria Gabriella; Longo,

Antonio; Ballinari, Dario

PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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KIND DATE
    PATENT NO.
                                        APPLICATION NO. DATE
                                         ______
    WO 9622976
                     A1
                           19960801
                                        WO 1995-EP5176 19951222
        W: AU, CA, JP, US
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                 AA
    CA 2186508
                           19960801
                                        CA 1995-2186508 19951222
    AU 9644363
                      A1
                           19960814
                                         AU 1996-44363
                                                          19951222
    AU 697673
                      В2
                           19981015
    EP 752985
                     A1
                           19970115
                                         EP 1995-943238
                                                         19951222
                         19990804
    EP 752985
                     В1
        R: CH, DE, ES, FR, GB, IT, LI, SE
     JP 09510993 T2 19971104
                                        JP 1995-522571 19951222
                     Т3
                                         ES 1995-943238 19951222
     ES 2137562
                           19991216
                                         IL 1996-116851 19960122
     IL 116851
                     A1
                           20000601
                                         US 1996-704760 19960925
    US 5840745
                     Α
                           19981124
PRIORITY APPLN. INFO.:
                                       GB 1995-1567 A 19950126
                                       WO 1995-EP5176 W 19951222
                       MARPAT 125:221574
OTHER SOURCE(S):
    For diagram(s), see printed CA Issue.
GI
AB
     3-Arylidene-2-oxindole derivs. [I; m = 0-2; A = (un) substituted bicyclic
     ring chosen from tetralin, naphthalene, quinoline and indole; R1 = H,
     alkyl, alkanoyl; one of R2 and R3 is H and the other is (un) substituted
     alkyl, (un) substituted alkoxycarbonyl, (un) substituted SO3H,
     (CH2) nN(alkyl)2, etc.; n = 2, 3], useful as tyrosine kinase
     inhibitors for the treatment of tumors, diabetic complications (no data),
     restenosis (no data), etc. (no data), are prepd. and I-contg. formulations
     presented. Thus, 3-carbethoxy-3-(5-methoxyindol-3-ylmethylene)-2-oxyndole
    was prepd. and demonstrated a IC50 of 1.99 .mu.M against v-abl
     tyrosine kinase and a IC50 of 2.34 .mu.M against the growth of
     K562 chronic myeloid leukemia cells.
ΙT
     181222-47-9P 181222-52-6P 181222-54-8P
     181222-56-0P 181222-58-2P 181222-60-6P
     181222-62-8P 181222-64-0P 181222-68-4P
     181222-70-8P 181222-72-0P 181222-73-1P
     181222-74-2P 181222-75-3P 181222-76-4P
     181222-77-5P 181222-78-6P 181222-79-7P
     181222-80-0P 181222-81-1P 181222-82-2P
     181222-84-4P 181223-06-3P 181223-07-4P
     181223-08-5P 181223-09-6P 181223-10-9P
     181223-12-1P 181223-14-3P 181223-16-5P
     181223-18-7P 181223-20-1P 181223-22-3P
     181223-24-5P 181223-26-7P 181223-28-9P
     181223-30-3P 181223-32-5P 181223-34-7P
     181223-35-8P 181223-37-0P 181223-39-2P
     181223-41-6P 181223-43-8P 181223-45-0P
     181223-47-2P 181223-48-3P 181223-49-4P
     181223-51-8P 181223-52-9P 181223-53-0P
     181223-55-2P 181223-56-3P 181223-57-4P
     181223-59-6P 181223-60-9P 181223-61-0P
     181223-62-1P 181223-63-2P 181223-80-3P
     181223-82-5P 181223-83-6P 181223-85-8P
     181223-86-9P 181223-87-0P 181223-89-2P
     181223-90-5P 181223-91-6P 181223-93-8P
     181223-94-9P 181223-96-1P 181223-98-3P
     181223-99-4P 181224-00-0P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
```

(prepn. of hydrosol. 3-arylidene-2-oxyindole tyrosine kinase

inhibitors)

RN 181222-47-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, methyl ester (9CI) (CA INDEX NAME)

RN 181222-52-6 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]-, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

● HCl

RN 181222-54-8 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]-, monohydrochloride, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} & H & \\ \hline & N & \\ N & \\ N & \\ \end{array}$$

● HCl

CN Benzenesulfonamide, 4-chloro-N-[3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181222-58-2 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-, ethyl ester (9CI) (CA INDEX NAME)

RN 181222-60-6 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ Ph-CH_2-NH-C & & \\ & & \\ O & & \\ \end{array}$$

RN 181222-62-8 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-y1)methylene]-2-oxo- (9CI) (CA INDEX NAME)

RN 181222-64-0 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H \\ \hline & N & C & N \\ \hline & N & N \\ \hline & N & N \\ \end{array}$$

# HCl

RN 181222-68-4 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

$$HO-CH_2-CH-CH_2-NH$$
 OH

RN 181222-70-8 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 181222-72-0 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

MeO 
$$\frac{1}{N}$$
  $\frac{1}{N}$   $\frac{1}{N}$ 

RN 181222-73-1 CAPLUS

CN Propanamide, N-[2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl]-2,3-dihydroxy-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OH} & \text{CH} \\ \text{HO-CH}_2\text{-CH-C-NH} & \text{CH} \\ \text{O} & \text{NH} \end{array}$$

RN 181222-74-2 CAPLUS

CN Methanesulfonamide, N-[2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181222-75-3 CAPLUS

CN Guanidine, [2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$H_2N-C-NH$$
 $NH$ 
 $NH$ 
 $NH$ 

$$H_2N-C-NH$$
 $NH$ 
 $NH$ 
 $NH$ 
 $NH$ 

RN 181222-76-4 CAPLUS

CN Urea, [2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ H_2N-C-NH & & & \\ & & & \\ O & & & NH \end{array}$$

RN 181222-77-5 CAPLUS

CN 2H-Indol-2-one, 5-(2,3-dihydroxypropoxy)-1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

RN 181222-78-6 CAPLUS

CN Acetic acid, hydroxy-, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl ester (9CI) (CA INDEX NAME)

RN 181222-79-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-(phosphonooxy)-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181222-80-0 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-, methyl ester (9CI) (CA INDEX NAME)

RN 181222-81-1 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-, monohydrochloride (9CI) (CA INDEX NAME)

HC1

RN 181222-82-2 CAPLUS

CN 2H-Indol-2-one, 5-(aminomethyl)-1,3-dihydro-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181222-84-4 CAPLUS

CN 2H-Indol-2-one, 5-(aminomethyl)-1,3-dihydro-3-(4-quinolinylmethylene)-, monohydrochloride (9CI) (CA INDEX NAME)

$$H_2N-CH_2$$
 $O$ 
 $O$ 
 $O$ 
 $O$ 

● HCl

RN 181223-06-3 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181223-07-4 CAPLUS
CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)(9CI) (CA INDEX NAME)

RN 181223-08-5 CAPLUS
CN 2H-Indol-2-one, 5-[bis(2-hydroxyethyl)amino]-1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ \text{HO-} \, \text{CH}_2 - \, \text{CH}_2 & & \text{CH} \\ \text{HO-} \, \text{CH}_2 - \, \text{CH}_2 - \, \text{N} & & & \\ \end{array}$$

RN 181223-09-6 CAPLUS
CN 1-Piperidinepropanamide, N-[2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-10-9 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181223-12-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-(hydroxymethyl)-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181223-14-3 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

RN 181223-16-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-

# (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H_{2N-S} \\
 & O \\$$

RN 181223-18-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, methyl ester (9CI) (CA INDEX NAME)

RN 181223-20-1 CAPLUS

CN 2H-Indol-2-one, 5-[bis(2-hydroxyethyl)amino]-1,3-dihydro-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

$$HO-CH_2-CH_2-N$$
 $HO-CH_2-CH_2$ 
 $HO-CH_2-CH_2$ 

RN 181223-22-3 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

OH 
$$CH_2-CH-CH_2-NH$$
  $CH$   $CH$ 

RN 181223-24-5 CAPLUS

CN Urea, [2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & H \\
H_2N-C-NH & CH & H
\end{array}$$

RN 181223-26-7 CAPLUS

CN Guanidine, [2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-28-9 CAPLUS

CN Propanamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-2,3-dihydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OH} & \text{O} \\ \text{OH} & \text{C} \\ \text{HO-CH}_2\text{-CH-C-NH} \end{array}$$

RN 181223-30-3 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-32-5 CAPLUS

CN Methanesulfonamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-34-7 CAPLUS

CN Acetamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-

2-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ \text{HO-} & \text{CH}_2 - \text{C-} & \text{NH} \end{array}$$

RN 181223-35-8 CAPLUS

CN 2H-Indol-2-one, 5-(2,3-dihydroxypropoxy)-1,3-dihydro-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} OH & H \\ HO-CH_2-CH-CH_2-O & CH \\ \end{array}$$

RN 181223-37-0 CAPLUS

CN 2H-Indol-2-one, 5-(aminomethyl)-1,3-dihydro-3-(1H-indol-3-ylmethylene)-(9CI) (CA INDEX NAME)

RN 181223-39-2 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ H_2N - C & \\ NH & \\ \end{array}$$

RN 181223-41-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-(hydroxymethyl)-3-(1H-indol-3-ylmethylene)-(9CI) (CA INDEX NAME)

RN 181223-43-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-5-(phosphonooxy)-(9CI) (CA INDEX NAME)

RN 181223-45-0 CAPLUS

CN 1H-Indole-5-sulfonic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

RN 181223-47-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H \\
 & N & CH & N \\
 & O & N & CH & N
\end{array}$$

RN 181223-48-3 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[bis(2-hydroxyethyl)amino]-1H-indol-3-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

HO-
$$CH_2$$
- $CH_2$ - $CH_2$ - $CH_2$ 

RN 181223-49-4 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[(2,3-dihydroxypropyl)amino]-1H-indol-3-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{OH} & & \\ & & \\ \text{HO-} \text{ CH}_2 - \text{ CH-} \text{ CH}_2 - \text{ NH} \end{array}$$

RN 181223-51-8 CAPLUS

CN Urea, [3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H & & O & H \\ \hline O & & & & N & \\ H_2N-C-NH & & & & CH & \\ \end{array}$$

RN 181223-52-9 CAPLUS

CN Guanidine, [3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H \\ NH & & \\ H2N-C-NH & & \end{array}$$

RN 181223-53-0 CAPLUS

CN Propanamide, N-[3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]-2,3-dihydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OH} & \text{O} \\ \text{OH} & \text{CH} \\ \end{array}$$

RN 181223-55-2 CAPLUS

CN 1-Piperidinepropanamide, N-[3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-56-3 CAPLUS

CN Methanesulfonamide, N-[3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & H \\
N & CH \\
Me-S-NH & O \\
M & O$$

RN 181223-57-4 CAPLUS

CN Acetic acid, hydroxy-, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-1H-indol-5-yl ester (9CI) (CA INDEX NAME)

RN 181223-59-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-(2,3-dihydroxypropoxy)-1H-indol-3-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H \\ & & & \\ \text{OH} \\ & & \\ \text{HO-CH}_2-\text{CH-CH}_2-\text{O} \end{array}$$

RN 181223-60-9 CAPLUS

CN 2H-Indol-2-one, 3-[[5-(aminomethyl)-1H-indol-3-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline H_2N-CH_2 & CH & \end{array}$$

RN 181223-61-0 CAPLUS

CN 1H-Indole-5-carboximidamide, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

$$H_2N-C$$
 $H_2N-C$ 
 $H_2N-C$ 

RN 181223-62-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-(hydroxymethyl)-1H-indol-3-yl]methylene]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline N & CH & \end{array}$$

RN 181223-63-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-(phosphonooxy)-1H-indol-3-yl]methylene]-(9CI) (CA INDEX NAME)

RN 181223-80-3 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

RN 181223-82-5 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-, ethyl ester (9CI) (CA INDEX NAME)

RN 181223-83-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 181223-85-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 181223-86-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

$$Ph-CH_2-O-C$$

$$OMe$$

RN 181223-87-0 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

$$Ph-CH_2-O-C$$

$$O$$

$$O$$

$$CH$$

$$CH$$

RN 181223-89-2 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-2-oxo-N-phenyl-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

RN 181223-90-5 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-N-phenyl- (9CI) (CA INDEX NAME)

RN 181223-91-6 CAPLUS

CN 1H-Indole-5-carboxamide, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-phenyl-(9CI) (CA INDEX NAME)

RN 181223-93-8 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-2-oxo-N-(phenylmethyl)-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 181223-94-9 CAPLUS

CN 1H-Indole-5-carboxamide, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

$$Ph-CH_2-NH-C$$

$$O$$

$$O$$

$$H$$

$$N$$

$$CH$$

$$H$$

$$N$$

$$CH$$

RN 181223-96-1 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-2-oxo-, ethyl ester (9CI) (CA INDEX NAME)

RN 181223-98-3 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-2-oxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} OH & \\ N & \\ CH & \\ CH & \\ NH & \\ \end{array}$$

RN 181223-99-4 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H \\ & & & \\ \text{OH} \\ & & \\ \text{HO-} \text{ CH}_2 - \text{CH-} \text{ CH}_2 - \text{NH} \end{array}$$

RN 181224-00-0 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H_{2N-C} & H_{N-C} & H_{N-C} \\ H_{2N-C} & H_{N-C} \\ H_{2N-C} & H_{N-C} & H_{N-C} \\ H_{2N-C} & H_{N-C} \\ H_{2N-C} & H_{N-C} & H_{N-C} \\ H_{2N-C} & H_{N-C} \\ H_{2N-C$$

IT 181224-02-2 181224-03-3 181224-04-4

181224-05-5

RL: RCT (Reactant)

(prepn. of hydrosol. 3-arylidene-2-oxyindole **tyrosine** kinase inhibitors)

RN 181224-02-2 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

RN 181224-03-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181224-04-4 CAPLUS

CN 1H-Indole-5-carbonitrile, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

RN 181224-05-5 CAPLUS

CN 2H-Indol-2-one, 5-(chloromethyl)-1,3-dihydro-3-(4-quinolinylmethylene)-(9CI) (CA INDEX NAME)

L5 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:209666 CAPLUS

DOCUMENT NUMBER: 124:260834

TITLE: Preparation and formulation of substituted

azaindolylidene compounds as tyrosine kinase

inhibitors

INVENTOR(S): Buzzetti, Franco; Brasca, Gabriella Maria; Longo,

Antonio; Ballinari, Dario

PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.				KIND		DATE			APPLICATION NO.						DATE			
WO 9600226				 Z	 1	19960104			WO 1995-EP2043 19950530									
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		RU,	SD,	SI,	SK,	ТJ,	TT,	UA,	US,	UZ,	VN							
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									CA 1995-2168659									
									AU 1995-26716									
EΡ	715628		A1 19960612				EP 1995-921777											
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	IT,		NL,		SE		
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				A2 19970128									1995					
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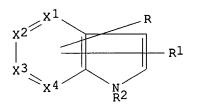
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                                                               19960222
PRIORITY APPLN. INFO.:
                                          GB 1994-12719
                                                               19940624
                                          WO 1995-EP2043
                                                               19950530
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OTHER SOURCE(S):

MARPAT 124:260834

Ι

GΙ



kinase inhibitors) 175075-26-0 CAPLUS

RN

CN

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AB
     The title compds. I [one of X1 , X2, X3, X4 is N and the others are CH; R
     is CH:C(CN)CONH2, etc.; R1 is hydrogen, amino, carboxy, cyano, etc.; R2 is
     H, C1-C6 alkyl, etc.; a proviso is given] are prepd. 5-Cyano-3-[(7-
     azaindol-3-yl)methylen]-2-oxindole (NMR data given) in vitro showed IC50
     of 0.98 mM against p-45 v-abl kinase.
TΤ
     175075-26-0P 175075-28-2P 175075-29-3P
     175075-30-6P 175075-31-7P 175075-32-8P
     175075-33-9P 175075-34-0P 175075-35-1P
     175075-36-2P 175075-37-3P 175075-38-4P
     175075-39-5P 175075-40-8P 175075-41-9P
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     175076-51-4P 175076-52-5P 175076-53-6P
     175076-54-7P 175076-55-8P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. of substituted azaindolylidene compds. as tyrosine
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1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-

ylmethylene) - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ H_2N-S \\ & & \\ & & \\ O \end{array}$$

RN 175075-28-2 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, ethyl ester (9CI) (CA INDEX NAME)

RN 175075-29-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, phenylmethyl ester (9CI) (CA INDEX NAME)

$$Ph-CH_2-O-C$$

$$O$$

$$O$$

$$CH$$

$$N$$

$$N$$

$$N$$

$$N$$

RN 175075-30-6 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-31-7 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{OH} & & \\ & & \\ \text{HO-} & \text{CH}_2 - \text{CH-} & \text{CH}_2 - \text{NH} \end{array}$$

RN 175075-32-8 CAPLUS

CN Propanamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]-2,3-dihydroxy- (9CI) (CA INDEX NAME)

RN 175075-33-9 CAPLUS

CN Methanesulfonamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & H & N \\
N & CH & N \\
Me-s-NH & O & N \\
N & O & N \\
N$$

RN 175075-34-0 CAPLUS

CN Guanidine, [2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & H & \\ NH & & & \\ H2N-C-NH & & & \\ \end{array}$$

RN 175075-35-1 CAPLUS

CN Urea, [2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H \\
 & N & C & NH
\end{array}$$

RN 175075-36-2 CAPLUS

CN 2H-Indol-2-one, 5-(2,3-dihydroxypropoxy)-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{OH} & & & \\ \text{HO-} \text{CH}_2\text{-} \text{CH-} \text{CH}_2\text{-} \text{O} & & \\ \end{array}$$

RN 175075-37-3 CAPLUS

CN Acetic acid, hydroxy-, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
& & & & \\
& & & \\
& & & \\
\text{HO-} & \text{CH}_2 - \text{C-} & & \\
\end{array}$$

RN 175075-38-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-(phosphonooxy)-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-39-5 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, methyl ester (9CI) (CA INDEX NAME)

RN 175075-40-8 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, monohydrochloride (9CI) (CA INDEX NAME)

$$H_2N-C$$
 $H_2N-C$ 
 $H_2N-C$ 
 $H_2N-C$ 

● HCl

RN 175075-41-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ \text{HO-} & \text{CH}_2 \\ \end{array} \\ \begin{array}{c} & \text{CH} \\ \end{array} \\ \begin{array}{c} & \text{H} \\ & \text{N} \\ \end{array} \\ \begin{array}{c} & \text{N} \\ & \text{N} \\ \end{array}$$

● HCl

RN 175075-42-0 CAPLUS

CN 1-Piperazineethanol, 4-[[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 175075-43-1 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-2-oxo-N-(phenylmethyl)-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

$$Ph-CH_2-NH-C$$

$$0$$

$$0$$

$$0$$

$$0$$

#### 09897755

RN 175075-44-2 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 175075-45-3 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]-, dihydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ N & \\ \end{array} \\ \begin{array}{c} CH_2 - CH_2 - C - NH \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} CH \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \\ \begin{array}{c} N \\ \end{array} \\ \\ \\ \begin{array}{c} N \\ \end{array} \\ \\$$

## ●2 HCl

RN 175075-46-4 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 157561-92-7 CMF C16 H12 N4 O

CM 2

CRN 76-05-1

CMF C2 H F3 O2

RN 175075-48-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 175075-47-5 CMF C17 H11 N3 O3

CM 2

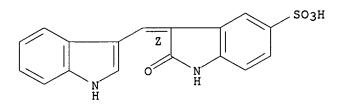
CRN 110-89-4 CMF C5 H11 N



RN 175075-96-4 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, monosodium salt, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



Na

RN 175075-97-5 CAPLUS

CN 1H-Indole-5-sulfonic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-

ylmethylene)-, monosodium salt, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

# Na

RN 175075-98-6 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175075-99-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-00-3 CAPLUS

CN Piperazine, 1-[[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-01-4 CAPLUS

CN Piperazine, 1-[[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]sulfonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-02-5 CAPLUS

CN 1-Piperazineethanol, 4-[[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]sulfonyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-03-6 CAPLUS

CN 1-Piperazineethanol, 4-[[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]sulfonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-04-7 CAPLUS

CN 2H-Indol-2-one, 5-[bis(2-hydroxyethyl)amino]-1,3-dihydro-3-(1H-indol-3-

Double bond geometry as shown.

RN 175076-05-8 CAPLUS

CN 2H-Indol-2-one, 5-[bis(2-hydroxyethyl)amino]-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-06-9 CAPLUS

CN Urea, [2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-07-0 CAPLUS

CN Urea, [2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN175076-08-1 CAPLUS

Guanidine, [2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-, CN (Z) - (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-09-2 CAPLUS

Guanidine, [2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-CN 1H-indol-5-yl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN

175076-10-5 CAPLUS
Propanamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-CN yl]-2,3-dihydroxy-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

175076-11-6 CAPLUS RN

CN Propanamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3ylmethylene)-1H-indol-5-yl]-2,3-dihydroxy-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-12-7 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-, dihydrochloride, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●2 HCl

RN 175076-13-8 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]-, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

●2 HCl

RN 175076-14-9 CAPLUS

CN Methanesulfonamide, N-[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-15-0 CAPLUS

CN Methanesulfonamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-16-1 CAPLUS

CN 2H-Indol-2-one, 5-(2,3-dihydroxypropoxy)-1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-17-2 CAPLUS

CN 2H-Indol-2-one, 5-(2,3-dihydroxypropoxy)-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-18-3 CAPLUS

CN Propanoic acid, 2,3-dihydroxy-, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-19-4 CAPLUS

CN Propanoic acid, 2,3-dihydroxy-, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-20-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-5-(phosphonooxy)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-21-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-(phosphonooxy)-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

RN 175076-22-9 CAPLUS

CN 2H-Indol-2-one, 5-(aminomethyl)-1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-23-0 CAPLUS

CN 2H-Indol-2-one, 5-(aminomethyl)-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-24-1 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-25-2 CAPLUS

CN 1H-Indole-5-carboximidamide, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-26-3 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-27-4 CAPLUS

CN 2H-Indol-2-one, 5-[(2,3-dihydroxypropyl)amino]-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-28-5 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, methyl ester, (Z)- (9CI) (CA INDEX NAME)

RN 175076-29-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-30-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-31-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-[[4-(2-hydroxyethyl)-1-piperazinyl]methyl]-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-32-1 CAPLUS

CN 1-Piperazineethanol, 4-[[2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl]carbonyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-33-2 CAPLUS

CN 1-Piperazineethanol, 4-[[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]carbonyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-34-3 CAPLUS

CN Acetic acid, hydroxy-, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-1H-indol-5-yl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-35-4 CAPLUS

CN Acetic acid, hydroxy-, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl ester, (E)- (9CI) (CA INDEX NAME)

## 09897755

RN 175076-37-6 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 175076-36-5

CMF C17 H13 N3 O

CDES 2: Z

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 175076-39-8 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 175076-38-7 CMF C16 H12 N4 O CDES 2:E

Double bond geometry as shown.

CM 2

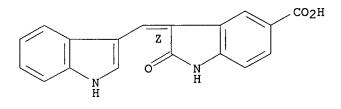
CRN 76-05-1 CMF C2 H F3 O2

RN 175076-41-2 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo, (Z)-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 175076-40-1 CMF C18 H12 N2 O3 CDES 2:Z

Double bond geometry as shown.



CM 2

CRN 110-89-4 CMF C5 H11 N



RN 175076-43-4 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)-, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM · 1

CRN 175076-42-3 CMF C17 H11 N3 O3 CDES 2:E

CM 2

CRN 110-89-4 CMF C5 H11 N



RN 175076-44-5 CAPLUS

CN 1H-Indole-5-carbonitrile, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-45-6 CAPLUS

CN 1H-Indole-5-carbonitrile, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-46-7 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, ethyl ester, (Z)- (9CI) (CA INDEX NAME)

RN 175076-47-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, ethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-48-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, phenylmethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-49-0 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, phenylmethyl ester, (E)- (9CI) (CA INDEX NAME)

RN 175076-50-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-, 2-phenylethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-51-4 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, 2-phenylethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-52-5 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-N-phenyl-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-53-6 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-2-oxo-N-phenyl-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

RN 175076-54-7 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-N-(phenylmethyl)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 175076-55-8 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-2-oxo-N-(phenylmethyl)-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c}
 & H \\
 & N \\
 & N \\
 & H
\end{array}$$

$$\begin{array}{c}
 & H \\
 & N \\
 & N \\
 & O
\end{array}$$

$$\begin{array}{c}
 & H \\
 & N \\
 & O
\end{array}$$

IT 157561-91-6 157561-92-7 175075-27-1 175075-47-5 175075-49-7 175075-50-0

RL: RCT (Reactant)

(prepn. of substituted azaindolylidene compds. as **tyrosine** kinase inhibitors)

RN 157561-91-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157561-92-7 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-27-1 CAPLUS

CN 1H-Indole-5-carbonitrile, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-47-5 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-49-7 CAPLUS

CN 2H-Indol-2-one, 5-(chloromethyl)-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 175075-50-0 CAPLUS

CN 1-Piperidinepropanamide, N-[2,3-dihydro-2-oxo-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

5 ANSWER 61 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:828284 CAPLUS

DOCUMENT NUMBER: 123:227985

TITLE: Arylidene and heteroarylidene oxindole derivatives as

tyrosine kinase inhibitors

INVENTOR(S): Buzzetti, Franco; Longo, Antonio; Brasca, Maria

Gabriella; Orzi, Fabrizio; Crugnola, Angelo;

Ballinari, Dario; Mariani, Mariangela Farmitalia Carlo Erba S.r.l., Italy

PATENT ASSIGNEE(S): Farmitalia Carlo Erba SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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					RU, SD, SK, UA, UZ, VN	
					GB, GR, IE, IT, LU, MC, NL, P	T, SE
					CA 1994-2142472 19940526	
AU	9469719	A1	19950124		AU 1994-69719 19940526	
AU	679754	B2	19970710			
EP	658159	A1	19950621		EP 1994-918379 19940526	
EP	658159	В1	20000823			
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FI	9500859	А	19950224		FI 1995-859 19950224	
RIORITY	APPLN.	INFO.:			GB 1993-13638 A 19930701	

EP 1994-918379 A3 19940526 WO 1994-EP1715 W 19940526

OTHER SOURCE(S):

MARPAT 123:227985

Ι

II

GΙ

$$(R^{10})_n$$
 $R^3 - Y - CH$ 
 $R^5$ 
 $R^5$ 
 $R^6$ 
 $R^6$ 
 $R^7$ 
 $R^4$ 

Title derivs. I [Y = naphthalene, tetralin, quinoline or isoquinoline system; R = H, plus oxo when Y is tetralin; R1, R2 independently = H, C1-6 alkyl or C2-6 alkanoyl; m = 0-2; n = 0-3; R3 independently = H, halo, cyano, C1-6 alkyl, carboxy, nitro or NR6R7 where R6, R7 independently = H, C1-6 alkyl; R5 = H, C1-6 alkyl] and their pharmaceutically acceptable salts, which are useful as tyrosine kinase inhibitors, are claimed. The E- and Z-isomers of approx. 85 compds. are specifically claimed. Several synthetic examples are given. For example, condensation of 8-hydroxyquinoline-5-carboxaldehyde with 5-hydroxy-2-oxindole in EtOH in the presence of piperidine at 60-70.degree. gave 60% title compd. II (R8 = OH). Among test results for 10 selected I for inhibition of p45 v-abl kinase in vitro, and for inhibition of cultured K562 human leukemia cell growth, II (R8 = Br) had IC50 values of 2.6 and 0.62 .mu.M, resp.

IT 149492-63-7P 168463-26-1P 168463-27-2P

149492-63-7P 168463-26-1P 168463-27-2P 168463-28-3P 168463-29-4P 168463-30-7P 168463-31-8P 168463-32-9P 168463-33-0P 168463-34-1P 168463-35-2P 168463-36-3P 168463-37-4P 168463-38-5P 168463-41-0P 168463-42-1P 168463-43-2P 168463-44-3P 168463-45-4P 168463-46-5P 168463-47-6P 168463-48-7P 168463-49-8P 168463-50-1P 168463-58-9P 168463-59-0P 168463-60-3P 168463-61-4P 168463-68-1P 168463-69-2P 168463-70-5P 168463-71-6P 168463-72-7P 168463-73-8P 168463-74-9P 168463-75-0P 168463-76-1P 168463-77-2P 168463-78-3P 168463-79-4P 168463-80-7P 168463-81-8P 168463-84-1P 168463-85-2P 168463-86-3P 168463-87-4P 168463-88-5P 168463-89-6P 168463-90-9P 168463-91-0P 168463-92-1P

Double bond geometry as shown.

RN 168463-26-1 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(5-quinolinylmethylene)-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-27-2 CAPLUS CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(5-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

RN 168463-28-3 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(5-quinolinylmethylene)-,
(E)- (9CL) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-29-4 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(4-quinolinylmethylene)-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-30-7 CAPLUS CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(4-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

RN 168463-31-8 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-32-9 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene], (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-33-0 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-2-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-34-1 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(8-hydroxy-4-quinolinyl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-35-2 CAPLUS CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-, (E)- (9CI) (CA INDEX NAME)

RN 168463-36-3 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-2-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-37-4 CAPLUS
CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene], (E)- (9CI) (CA INDEX NAME)

RN 168463-38-5 CAPLUS

CN 2H-Indol-2-one, 5-fluoro-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-41-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-7-quinolinyl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-42-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-4-quinolinyl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-43-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-44-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-45-4 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-46-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(2-methyl-1H-indol-3-yl)methylene]-, (E)- (9CI) (CA INDEX NAME)

RN 168463-47-6 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(2-methyl-1H-indol-3-yl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-48-7 CAPLUS
CN 1H-Indole-5-carbonitrile, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl], (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-49-8 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-1H-indol-3-yl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-50-1 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (E)-

## (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-58-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(8-hydroxy-5-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 168463-59-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-7-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 168463-60-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(2-methyl-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 168463-61-4 CAPLUS

CN 2H-Indol-2-one, 5-fluoro-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene](9CI) (CA INDEX NAME)

RN 168463-68-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(5-quinolinylmethylene)-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-69-2 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(5-quinolinylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

$$H_2N$$

RN 168463-70-5 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(5-quinolinylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

RN 168463-71-6 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(4-quinolinylmethylene)-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-72-7 CAPLUS CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(4-quinolinylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-73-8 CAPLUS
CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-(4-quinolinylmethylene)-,
(Z)- (9CI) (CA INDEX NAME)

RN 168463-74-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(8-hydroxy-5-quinolinyl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-75-0 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-76-1 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-2-oxo-, (Z)- (9CI) (CA INDEX NAME)

RN 168463-77-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(8-hydroxy-4-quinolinyl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-78-3 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-79-4 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-2-oxo-, (Z)- (9CI) (CA INDEX NAME)

RN 168463-80-7 CAPLUS CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-81-8 CAPLUS
CN 2H-Indol-2-one, 5-fluoro-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene], (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168463-84-1 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-7-quinolinyl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

RN 168463-85-2 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-4-quinolinyl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-86-3 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-4-quinolinyl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-87-4 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

RN 168463-88-5 CAPLUS
CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene], (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c|c} \text{MeO} \\ \hline \\ N \\ H \end{array}$$

RN 168463-89-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(2-methyl-1H-indol-3-yl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-90-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(2-methyl-1H-indol-3-yl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-91-0 CAPLUS

CN 1H-Indole-5-carbonitrile, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, (Z)- (9CI) (CA INDEX NAME)

RN 168463-92-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-1H-indol-3-yl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168463-93-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168464-10-6 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 168464-11-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(2-methyl-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 168464-12-8 CAPLUS

CN 1H-Indole-5-carbonitrile, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

RN 168464-13-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 168464-14-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 168464-15-1 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene](9CI) (CA INDEX NAME)

RN 168464-16-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 168464-17-3 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-(9CI) (CA INDEX NAME)

L5 ANSWER 62 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:518515 CAPLUS

DOCUMENT NUMBER: 123:227945

TITLE: Synthesis and configuration of some new bicyclic

3-arylidene-and 3-heteroarylidene-2-oxindoles Buzzetti, Franco; Pinciroli, Vittorio; BRasca, M.

AUTHOR(S): Buzzetti, Franco; Pinciroli, Vittorio; BRasca, M.

Gabriella; Crugnola, Angelo; Fustinoni, Silvia; Longo,

Antonio

CORPORATE SOURCE: Pharmacia, Farmitalia Carlo Erba S.R.L., Ricerca e

Sviluppo, Milano, I-20159, Italy

SOURCE: Gazz. Chim. Ital. (1995), 125(2), 69-75

CODEN: GCITA9; ISSN: 0016-5603

DOCUMENT TYPE: Journal LANGUAGE: English

AB The synthesis of a novel bicyclic 3-arylidene- and 3-heteroarylidene-2-oxindoles was described. Compds. 1-16 have been prepd. by condensation of 2-oxindole with a (hetero)arom. aldehyde belonging to the naphthtalene, tetralin, quinoline or indole series. Said indolones are expected to possessing tyrosine kinase inhibitory activity (no data). The singel E or Z isomers could be partially transformed into their isomers by acid or basic catalysis. The E/Z configuration assignment was achieved by

1H NMR spectroscopy on the basis of chem. shifts and NOE data obtained from NOESY spectra.

IT 149492-60-4P 149492-61-5P 149492-62-6P 149492-64-8P 168141-97-7P 168142-05-0P 168142-06-1P 168142-07-2P 168142-08-3P 168142-09-4P 168142-10-7P 168142-16-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and configuration of (arylidene)indolones)

RN 149492-60-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-hydroxy-2-quinolinyl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-61-5 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-(4-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-62-6 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (E)(9CI) (CA INDEX NAME)

RN 149492-64-8 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168141-97-7 CAPLUS
CN 2H-Indol-2-one, 3-[(5-amino-1H-indol-3-yl)methylene]-1,3-dihydro-, (Z)(9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$H_2N$$
 $N$ 
 $H$ 

RN 168142-05-0 CAPLUS
CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168142-06-1 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-nitro-1H-indol-3-yl)methylene]-, (Z)-

## (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168142-07-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168142-08-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-quinolinylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168142-09-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5,6,7,8-tetrahydro-2-quinolinyl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 168142-10-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (Z)-

## (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

RN 168142-16-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-quinolinylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L5 ANSWER 63 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:557633 CAPLUS

DOCUMENT NUMBER: 121:157633

TITLE: Preparation and formulation of azaindoles as

tyrosine kinase inhibitors

INVENTOR(S): Buzetti, Franco; Crugnola, Angelo; Ballinari, Dario;

Greco, Felicita

PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.R.L., Italy

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND			ND	DATE			A	PPLI	CATI	ои ис	DATE						
WO	WO 9414808 A1			1	1994	0707		WO 1993-EP3536 19931215									
	W:	ΑU,	BB,	BG,	BR,	BY,	CA,	CZ,	FI,	HU,	JP,	KP,	KR,	ΚZ,	LK,	MG,	MN,
		MW,	NO,	NZ,	PL,	RO,	RU,	SK,	UA,	VN							
	RW:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE
CA	2126	228		A.	A	19940707			CA 1993-2126228 19931215								
AU	94583	105		A.	1	1994	0719		Αl	J 199	94-5	8105		1993	1215		

AU 670488	B2	19960718			
EP 626963	A1	19941207		EP 1994-903774	19931215
EP 626963	B1	19990609			
R: AT, BE, C	H, DE,	DK, ES, FR	R, GE	B, GR, IE, IT, LI	, NL, PT, SE
HU 67431	A2	19950428		HU 1994-1950	19931215
JP 07504208	T2	19950511		JP 1993-514761	19931215
AT 181074	E	19990615		AT 1994-903774	19931215
ES 2134926	Т3	19991016		ES 1994-903774	19931215
IL 108087	A1	19970930		IL 1993-108087	19931220
ZA 9309578	Α	19940811		ZA 1993-9578	19931221
CN 1093707	Α	19941019		CN 1993-112970	19931222
US 5397787	Α	19950314		US 1993-171154	19931222
FI 9403838	Α	19940819		FI 1994-3838	19940819
PRIORITY APPLN. INFO.:			GB	1992-26855	19921223
			WO	1993-EP3536	19931215
OTHER SOURCE(S).	MAT	PAT 121 ⋅ 157	1633		

OTHER SOURCE(S): MARPAT 121:157633

GΙ

Title compds. [I; R2 = H, alkyl, alkanoyl; 1 of X1-X4 = N and the others are CH; any C may be substituted by R or R1; R = CH:C(CN)R6, (un)substituted 2-oxo-3-indolylidenemethylene; R1 = H, halo, alkyl(oxy), NO2, (di)(alkyl)amino; R6 = CONH2, CONH(CH2)nPh, CSNH2, cyano; n = 0-5] were prepd. Thus, 7-azaindole was formylated and the product refluxed with 2-oxindole in EtOH contg. piperidine to give (Z)-3-[(7-azaindol-3-yl)methylene]-2-oxindole which had IC50 of 0.05 .mu.M against p45 v-abl kinase in vitro.

IT 157561-89-2P 157561-91-6P 157561-92-7P 157561-93-8P 157561-94-9P 157561-95-0P 157561-96-1P 157562-04-4P 157562-05-5P 157562-10-2P 157562-11-3P 157562-16-8P 157562-17-9P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as tyrosine kinase inhibitor)

RN 157561-89-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 157561-91-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157561-92-7 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157561-93-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(1-methyl-1H-pyrrolo[2,3-b]pyridin-3-yl)methylene]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 157561-94-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine, 1-acetyl-3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 157561-95-0 CAPLUS

CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 157561-96-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-methoxy-1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 157562-04-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrolo[2,3-c]pyridin-3-ylmethylene)(9CI) (CA INDEX NAME)

RN 157562-05-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-pyrrolo[2,3-c]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157562-10-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrolo[3,2-c]pyridin-3-ylmethylene)(9CI) (CA INDEX NAME)

RN 157562-11-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-pyrrolo[3,2-c]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157562-16-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrolo[3,2-b]pyridin-3-ylmethylene)-(9CI) (CA INDEX NAME)

RN 157562-17-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-pyrrolo[3,2-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

IT 157562-18-0 157562-19-1 157562-20-4

RL: RCT (Reactant)

(reaction of, in prepn. of tyrosine kinase inhibitor)

RN 157562-18-0 CAPLUS

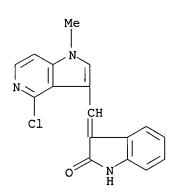
CN 2H-Indol-2-one, 1,3-dihydro-5-methoxy-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157562-19-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-(1H-pyrrolo[2,3-b]pyridin-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 157562-20-4 CAPLUS

CN 2H-Indol-2-one, 3-[(4-chloro-1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



L5 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:508407 CAPLUS

DOCUMENT NUMBER: 119:108407

TITLE: Cinnamamide analogs as inhibitors of protein

tyrosine kinases

AUTHOR(S): Buzzetti, Franco; Brasca, M. Gabriella; Crugnola,

Angelo; Fustinoni, Silvia; Longo, Antonio; Penco, Sergio; Dalla Zonca, Paolo; Comoglio, Paolo M.

CORPORATE SOURCE: Farmitalia Carlo Erba SRL, Milan, 20159, Italy

SOURCE: Farmaco (1993), 48(5), 615-36

CODEN: FRMCE8

DOCUMENT TYPE: Journal LANGUAGE: English

Protein tyrosine kinases (PTK) are important signal transducing AΒ enzymes involved in the modulation of normal cellular growth and differentiation and have been assocd. with the etiol. of various human cancers. The development of properly designed inhibitors, which block their function by interfering with the substrate binding, may therefore offer an unique target for selective anticancer chemotherapy. Here, the authors describe synthesis and biochem. testing of a novel series of non-peptide PTK inhibitors which have as characteristic active pharmacophore the cinnamamide moiety. For testing, the authors used an exogenous substrate kinase assay based on the phosphorylation of (Val5)-angiotensin II with radiolabeled ATP by the catalytic domain of the PTK encoded by the v-abl oncogene (p45 v-abl). The most potent compds. were found in the class of 3-arylidene-2-oxindoles (II) with IC50 values in the 1 .mu.M range. Among these, the 2-tetralylmethylene-, 4-quinolylmethylene-, 5-quinolylmethylene- and 3-indolylmethylene-2oxindole compds. were selected for further investigation.

IT 137478-40-1P 148563-43-3P 149492-59-1P 149492-60-4P 149492-61-5P 149492-62-6P

149492-63-7P 149492-64-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as protein tyrosine kinase inhibitor, structure in relation to)

RN 137478-40-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-quinolinylmethylene)- (9CI) (CA INDEX NAME)

RN 148563-43-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 149492-59-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-60-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-hydroxy-2-quinolinyl)methylene]-, (Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-61-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-quinolinylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-62-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]-, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-63-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(8-hydroxy-5-quinolinyl)methylene]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 149492-64-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-3-ylmethylene)-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L5 ANSWER 65 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:449225 CAPLUS

DOCUMENT NUMBER: 119:49225

TITLE: Methyleneoxindole derivatives and process for their

preparation

INVENTOR(S): Buzzetti, Franco; Longo, Antonio; Colombo, Maristella

PATENT ASSIGNEE(S): Farmitalia Carlo Erba Srl, Italy

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT NO.		KIND	DATE		APPLICATION NO.	DATE			
WO				19930121 , JP, KR,		WO 1992-EP1569	19920710			
						GB, GR, IT, LU, MC	, NL, SE			
						IL 1992-102383				
CA	CA 2091058			19930113		CA 1992-2091058	19920710			
EP				19930203		EP 1992-111757	19920710			
				19930224						
	R: PT									
AU	9222777		A1	19930211		AU 1992-22777	19920710			
				19950119						
						ZA 1992-5169	19920710			
EP	552329		A1	19930728		EP 1992-914619	19920710			
EP	552329		B1	20011004						
						GB, GR, IT, LI, NL				
JP	06501494		Т2	19940217		JP 1993-501981	19920710			
JP				20010716						
						ни 1993-723				
RU	2072989		C1	19970210		RU 1993-4893 AT 1992-914619	19920710			
US	5409949		Α	19950425		US 1993-987280				
PRIORIT	Y APPLN.	INFO	. :		(	GB 1991-15160 A				
				•	-	NO 1992-EP1569 A	19920710			
OTHER S	OURCE(S):		MA	RPAT 119:	49225	5				

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$$R_{2}$$
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 $R_{8}$ 

The title compds. I [R = II; R4 = H, OH, C1-6 alkoxy, C2-6 alkanoyloxy, C02H, N02, NHR7 (R7 = H, C1-6 alkyl); R5 = H, C1-6 alkyl or halo; R6 = H, C1-6 alkyl; n = 0-2; R1 = H, C1-6 alkyl, C2-6 alkanoyl; R2 = H, C1-6 alkyl, halo, CN, C02H, N02, NHR7; R3 = H, C1-6 alkyl, C2-6 alkanoyl] were prepd. by condensation of aldehydes III with oxindoles IV, and were evaluated as tyrosine kinase inhibitors. Thus, a soln. of 145

mg 3-indolecarboxaldehyde, 149 mg 5-hydroxy-2-oxindole, and 60 mg piperidine in 10 mL abs. EtOH was heated for 3 h at 60.degree.; workup afforded 60% I (R in 3-position, n = 0, R2 = R3 = R5 = R6 = H, R4 = 5-OH) (V). IC50 (.mu.M) values for V of 0.4 were detd. for both the myelin basic protein phosphorylation assay and the autophosphorylation assay. A 0.150 g tablet formulation contg. 25 mg active substance and lactose, corn starch, talc powder, and magnesium stearate is given.

IT 148563-46-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and acylation of, as tyrosine kinase inhibitor)

RN 148563-46-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(5-hydroxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

IT 148563-55-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and deetherification of, as tyrosine kinase inhibitor)

RN 148563-55-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-methoxy-3-[(5-methoxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

IT 148563-43-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and tyrosine kinase inhibiting activity of)

RN 148563-43-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 22813-84-9 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(1-methyl-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 148563-44-4 CAPLUS CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo(9CI) (CA INDEX NAME)

RN 148563-45-5 CAPLUS CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-indol-3-ylmethylene)- (9CI) (CA INDEX NAME)

RN 148563-47-7 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(7-hydroxy-1H-indol-3-yl)methylene]- (9CI) (CA INDEX NAME)

RN 148563-48-8 CAPLUS
CN 2H-Indol-2-one, 3-[(5,7-dihydroxy-1H-indol-3-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 148563-49-9 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5-hydroxy-1H-indol-3-yl)methylene]-(9CI) (CA INDEX NAME)

RN 148563-50-2 CAPLUS

CN 2H-Indol-2-one, 3-[(5-amino-1H-indol-3-yl)methylene]-1,3-dihydro-5-hydroxy-(9CI) (CA INDEX NAME)

RN 148563-51-3 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(5-hydroxy-1H-indol-3-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

RN 148563-52-4 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-5-hydroxy-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

RN 148563-53-5 CAPLUS

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(7-hydroxy-1H-indol-3-yl)methylene](9CI) (CA INDEX NAME)

RN 148563-54-6 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[(7-hydroxy-1H-indol-3-yl)methylene]-2-oxo- (9CI) (CA INDEX NAME)

RN 148563-56-8 CAPLUS

CN 2H-Indol-2-one, 5-(acetyloxy)-3-[[5-(acetyloxy)-1H-indol-3-yl]methylene]1,3-dihydro- (9CI) (CA INDEX NAME)

RN 148563-57-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 3-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]- (9CI) (CA INDEX NAME)

RN 148563-58-0 CAPLUS

CN 2H-Indol-2-one, 3-[(5-amino-1H-indol-3-yl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN148563-59-1 CAPLUS 2H-Indol-2-one, 1,3-dihydro-3-[(5-nitro-1H-indol-3-yl)methylene]- (9CI) CN (CA INDEX NAME)

ANSWER 66 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1991:679621 CAPLUS

DOCUMENT NUMBER:

115:279621

TITLE:

Preparation of (hetero)arylacrylates useful as

tyrosine kinase inhibitors

INVENTOR(S):

Buzzetti, Franco; Longo, Antonio; Colombo, Maristella

Farmitalia Carlo Erba S.r.l., Italy

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.		KIND	DATE		APPLICATION NO.	DATE
WO	9113055		A2	19910905		WO 1991-EP350	19910226
WO	9113055		A3	19911031			
	W: AU,	CA,	FI, HU	, JP, KR,	SU,	US	
	RW: AT,	BE,	CH, DE	, DK, ES,	FR,	GB, GR, IT, LU, NL	, SE
IL	97049		A1	19951031		IL 1991-97049	19910125
CA	2053253		AA	19910829		CA 1991-2053253	19910226
ΑU	9172412		A1	19910918		AU 1991-72412	19910226
ΑU	652740		В2	19940908			
EΡ	470221		A1	19920212		EP 1991-904125	19910226
EΡ	470221		В1	19951213			
	R: AT,	BE,	CH, DE	, DK, ES,	FR,	GB, GR, IT, LI, NL	, SE
HU	59081		A2	19920428		HU 1991-3626	19910226
HU	210791		В	19950728			
JP	04506081		Т2	19921022		JP 1991-504222	19910226

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JP 3152434
                       B2
                             20010403
                                            EP 1995-102495
     EP 662473
                       A1
                             19950712
                                                              19910226
     EP 662473
                             19990901
                       В1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE
                             19951215
                                            AT 1991-904125
                                                              19910226
    AT 131470
                       Ε
     ES 2083569
                             19960416
                                            ES 1991-904125
                                                              19910226
                       Т3
     RU 2091369
                                            RU 1991-5010251
                       C1
                             19970927
                                                              19910226
    AT 184000
                       Ε
                             19990915
                                            AT 1995-102495
                                                              19910226
     ES 2137386
                       Т3
                             19991216
                                            ES 1995-102495
                                                              19910226
     JP 2000204070
                       A2
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                                            JP 2000-40167
                                                              19910226
     ZA 9101441
                       Α
                             19911127
                                            ZA 1991-1441
                                                              19910227
    US 5374652
                       Α
                             19941220
                                            US 1993-126687
                                                              19930927
                                            US 1994-294350
    US 5488057
                       Α
                             19960130
                                                              19940823
                                            US 1995-455688
                             19970506
    US 5627207
                       Α
                                                              19950531
                                         GB 1990-4483
                                                           A 19900228
PRIORITY APPLN. INFO .:
                                         EP 1991-904125
                                                           A3 19910226
                                         JP 1991-504222
                                                           A3 19910226
                                         WO 1991-EP350
                                                           A 19910226
                                         US 1991-768259
                                                           B1 19911028
                                         US 1993-126687
                                                           A3 19930927
                                         US 1994-294350
                                                           A3 19940823
                         MARPAT 115:279621
OTHER SOURCE(S):
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$$CH = C (CN) CSNH_{2}$$

$$OH$$

$$CH = C (CN) CONH_{2} II$$

$$CH = C (CN) CONH_{2} III$$

Title compds., useful in treatment of cancer and other pathol. AΒ proliferative conditions (no data), are prepd. 2-Hydroxy-1naphthaldehyde, NCCH2CSNH2, HOCH2CH2NEt2, and EtOH were refluxed 30 min to give naphthylthioacrylamide I. Prepd. similarly were quinolineacrylamide II and quinolylmethyleneoxindole III. A capsule and tablet formulation contg. 2-cyano-3-(3-hydroxynaphth-2-yl)acrylamide and 2-cyano-3-(1hydroxynaphth-2-yl)acrylamide, resp.

ΙT 137478-38-7P 137478-39-8P 137478-40-1P 137479-18-6P 137479-19-7P 137479-20-0P 137479-21-1P 137501-13-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as tyrosine kinase inhibitor)

137478-38-7 CAPLUS RN

2H-Indol-2-one, 1,3-dihydro-3-(2-quinolinylmethylene)- (9CI) (CA INDEX CN NAME)

RN 137478-39-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(4-hydroxy-2-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 137478-40-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-quinolinylmethylene)- (9CI) (CA INDEX NAME)

RN 137479-18-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(7-hydroxy-3-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 137479-19-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-5-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 137479-20-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(7-hydroxy-6-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 137479-21-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-6-quinolinyl)methylene]- (9CI) (CA INDEX NAME)

RN 137501-13-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

ANSWER 1 OF 66 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:275806 CAPLUS DOCUMENT NUMBER: 136:304047 TITLE: Effects of combined administration of farnesyl transferase inhibitors and signal transduction inhibitors Daley, George Q.; Hoover, Russell R. INVENTOR(S): Whitehead Institute for Biomedical Research, USA PATENT ASSIGNEE(S): PCT Int. Appl., 30 pp. CODEN: PIXXD2 Patent DOCUMENT TYPE: English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: APPLICATION NO. DATE PATENT NO. KIND DATE \_\_\_\_\_ \_\_\_\_ WO 2002028409 A2 20020411 WO 2001-US31104 20011004 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRIORITY APPLN. INFO.: US 2000-238240P P 20001005 US 2000-238813P P 20001006 The invention relates to methods of reducing proliferation of cells, AΒ enhancing apoptosis of cells or both in an individual in need thereof, comprising administering to the individual a combination of at least one farnesyl transferase inhibitor (FTI), such as an inhibitor or Ras function, and at least one signal transduction inhibitor (STI) in a therapeutically effective amt., wherein proliferation of cells is reduced and/or apoptosis of cells in enhanced in the individual. The invention also discloses a method of reducing proliferation of STI resistant cells, enhancing apoptosis of STI resistant cells, or both in an individual in need thereof, comprising administering to the individual a combination of at least one FTI and at least one STI in a therapeutically effective amt., wherein proliferation of STI resistant cells is reduced and/or apoptosis of STI resistant cells is enhanced in the individual. The invention can be used to treat leukemia (e.g., CML) using this combination of farnesyl transferase inhibitor and signal transduction inhibitor. 204005-46-9, SU5416 IΤ RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (effects of combined administration of farnesyl transferase inhibitors

2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-

and signal transduction inhibitors)

204005-46-9 CAPLUS

(9CI) (CA INDEX NAME)

RN

CN

L5 ANSWER 2 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:131838 CAPLUS

TITLE: The total synthesis of proteasome inhibitors TMC-95A

and TMC-95B: discovery of a new method to generate

cis-propenyl amides

AUTHOR(S): Lin, Songnian; Danishefsky, Samuel J.

CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan - Kettering

Institute for Cancer Research, New York, NY, 10021,

USA

SOURCE: Angewandte Chemie, International Edition (2002),

41(3), 512-515

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Total synthesis of proteasome inhibitors TMC-95A and TMC-95B (I; A =AB S-side chain, B = R-side chain) was accomplished using a stereo-specific generation of the (Z)-propenamide side chain developed for the purpose. Silatropic bond reorganization of 1-silylated-2-propen-1-amides (II; R = Ph, 4-MeO-C6H4, 2-furyl, (CH3)3CCH2-, Boc-Ser(SiiPr3)-) occurred when the compds. were heated at .apprx.110.degree. for from 10 h - 4 days to give the corresponding (Z)-1-propenamides in yields of 52-81%. The total synthesis began with crossed-aldol condensation of 8-iodo-2-oxo-indole and Garner aldehyde (III); the (Z) isomer of the resulting E/Z mixt. of product (IV) could be isomerized to (E) using iodine. L-Lys was elaborated into reactant (V), which was Suzuki-coupled to E-IV, the product coupled with H-Asn-OBut, and the product was converted to the dihydroxy compd., which, after protection/deprotection steps, was macrolactamized to give the core structure. Acylation of free amine with (.+-.)-3-methyl-2-oxo-pentanoic acid gave the mixt. of A/B product precursors, which were then reacted with H2NCH(SiEt3)CH:CH2 and the product subjected to the above thermal rearrangement to give the protected I. Global deprotection followed by RP-HPLC sepn. yielded I, which were characterized by comparison of their high-field NMR spectra with authentic samples.

IT INDEXING IN PROGRESS

IT 421556-66-3P 421556-67-4P 421556-70-9P 421556-71-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of TMC-95A and -B using a thermal silatropic bond reorganization to generate the Z-propenamide side-chain)

RN 421556-66-3 CAPLUS

CN 3-Oxazolidinecarboxylic acid, 4-[(E)-(1,2-dihydro-7-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,2-dimethyl-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 421556-67-4 CAPLUS

CN 3-Oxazolidinecarboxylic acid, 4-[(Z)-(1,2-dihydro-7-iodo-2-oxo-3H-indol-3-ylidene)methyl]-2,2-dimethyl-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 421556-70-9 CAPLUS

CN 3-Oxazolidinecarboxylic acid, 4-[(E)-[1,2-dihydro-7-[5-[(2S)-3-methoxy-3-oxo-2-[((phenylmethoxy)carbonyl]amino]propyl]-2-(phenylmethoxy)phenyl]-2-oxo-3H-indol-3-ylidene]methyl]-2,2-dimethyl-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

RN 421556-71-0 CAPLUS

CN L-Asparagine, 3-[(3E)-3-[(4S)-3-[(1,1-dimethylethoxy)carbonyl]-2,2-dimethyl-4-oxazolidinyl]methylene]-2,3-dihydro-2-oxo-1H-indol-7-yl]-N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-tyrosyl-, 1,1-dimethylethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

REFERENCE COUNT:

THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 66 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:43419 CAPLUS

DOCUMENT NUMBER:

136:259310

AUTHOR(S):

TITLE: The antiangiogenic agents SU5416 and SU6668 increase

the antitumor effects of fractionated irradiation Ning, Shoucheng; Laird, Douglas; Cherrington, Julie

M.; Knox, Susan J.

CORPORATE SOURCE: Department of Radiation Oncology, Stanford University

Medical Center, Stanford, CA, 94305-5105, USA

SOURCE: Radiation Research (2002), 157(1), 45-51

CODEN: RAREAE; ISSN: 0033-7587

PUBLISHER: Radiation Research Society

DOCUMENT TYPE: Journal LANGUAGE: English

Angiogenesis is crit. for tumor development, growth and metastasis. vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF) and their tyrosine kinase receptors are major regulators of angiogenesis. Radiation induces the prodn. of VEGF, FGF and PDGF in many tumor cells. We hypothesized that inhibition of the function of these growth factors could inhibit tumor angiogenesis and thereby enhance the efficacy of radiation therapy. To test this hypothesis, we used the small mol. inhibitors SU5416 (an inhibitor for Vegf receptor) and SU6668 (an inhibitor for Vegf, Fgf and Pdgf receptors) alone and in combination with fractionated irradn. to treat C3H mice bearing SCC VII carcinomas. The SCC VII tumors express Vegf, Fgf2 (also known as bFGF), Pdgf and their assocd. receptors. Animals were given either SU5416 or SU6668 daily before or after irradn. (2 Gy per fraction per day for 5 days). The results from these expts. demonstrate that administration of either SU5416 or SU6668 without radiation delayed tumor growth. Administration of SU5416 at a dose of 25 mg/kg per day (the max. tolerated ED) inhibited tumor growth by 17.9% on day 7 (P < 0.05 compared to untreated control mice) and produced an av. tumor growth delay time of 0.5-2.0 days. When combined with fractionated irradn., administration of SU5416 increased the inhibition of tumor growth to 50-53% on day 7 and the tumor growth delay time to 5.7-6.5 days (P < 0.001 compared with SU5416 alone; P 0.05 compared with radiation alone). SU6668 alone inhibited tumor growth in a dose-dependent manner. Administration of SU6668 at a dose of 75 mg/kg per day (a suboptimal dose) inhibited tumor growth by 36% on day 7 and produced an av. tumor growth delay time of 3.3 .+-. 1.4 days. The combination of SU6668 with fractionated radiation increased inhibition of tumor growth to 66-70% and the tumor growth delay time from 3.3 days to 11.9 days (P.ltoreq. 0.001 compared with either radiation alone or SU6668 alone). Administration of these agents before or after irradn. produced similar results (P = 0.40for SU5416; P = 0.98 for SU6668). SU5416 or SU6668 alone or in combination with radiation was very well tolerated with little or no toxicity. These results suggest that inhibition of Vegf, Fgf and Pdgf receptor function by SU5416 and SU6668 can enhance the efficacy of irradn. The targeting of multiple tyrosine kinase receptors by SU6668 is more effective than inhibition of the Vegf receptor alone by SU5416 for the enhancement of tumor cell killing by fractionated irradn.

IT 204005-46-9, SU5416

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiangiogenic agents SU5416 and SU6668 increase antitumor effects of fractionated irradn.)

RN 204005-46-9 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 66 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:31440 CAPLUS

DOCUMENT NUMBER: 136:102386

Preparation and use of 4-heteroaryl-3-heteroarylidenyl-TITLE:

2-indolinones and their use as protein kinase

inhibitors

Tang, Peng Cho; Wei, Chung Chen; Huang, Ping; Cui, INVENTOR(S):

Jingron

Sugen, Inc., USA PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 164 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

GΙ

	PATENT NO.			KI	KIND DA		DATE			APPLICATION NO.					DATE				
	WO 2002002551			- <b>-</b>	 1	20020110		WO 2001-US2076			68 20010629								
	. W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,		
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,		
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,		
		RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,		
		UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM				
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	ΒE,	CH,	CY,		
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,		
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG				
PRIORITY APPLN. INFO.:				US 2000-215654P P 20000630															
	OTHER SOURCE	(S):			MARPAT 136:102386														
GT																			

Title compds. I [R1-2 = H, alkyl, cycloalkyl, aryl, heteroaryl, AΒ heteroalicyclic, halo, etc.; Het = (un)substituted arom. heterocycle

II

TΤ

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contg. at least one and not more than two N atoms,
tetrahydro(thio)pyranyl, (thio)morpholino, piperidinyl, piperazinyl,
tetrazolyl, etc.; Q = (un)substituted arom. heterocycle contg. not more
than two N atoms, 5-membered ring (un) substituted heterocycle contg. N, O
or S, e.g., imidazolyl, pyrrolyl, indolyl, etc.] with some exceptions,
were prepd. Included are 75 synthetic examples and results for several
protein tyrosine kinase assays for those compds. For instance,
4-bromoindole was coupled to bis(pinacolato)diborane (DMSO, KOAc,
PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 22 h). The resulting dioxaborolane was coupled to 4-bromopyridine.bul.HCl (THF, Pd(PPh3)4, NaOH, 70.degree.C,
6 h) to give the indole which was treated with C5H5N.bul.Br3
(t-BuOH/EtOH/H2O, 1h) followed by zinc (stirred 1 addnl. hour) to give
4-(pyridin-4-yl)-1,3-dyhydroindol-2-one as a yellow solid. Condensation
of this intermediate with 5-methylimidazole-4-carboxaldehyde (EtOH,
piperidine, 2 days) afforded II. II had IC50 = 4.88 mM for FGFR-1
tyrosine kinase and 0.03 mM for cdk2/cyclin A tyrosine
kinase. I are useful in treating cancer, immunol. disorders, etc.
388116-44-7P 388116-45-8P 388116-46-9P
388116-47-0P 388116-50-5P 388116-51-6P
388116-52-7P 388116-54-9P 388116-55-0P
388116-56-1P 388116-57-2P, 3-(1H-Indol-2-ylmethylene)-4-
(pyridin-4-yl)-1,3-dihydroindol-2-one 388116-58-3P,
4-(Pyridin-4-yl)-3-(4,5,6,7-tetrahydro-1H-indol-2-ylmethylene)-1,3-
dihydroindol-2-one 388116-59-4p, 3-[5-(2-(Morpholin-4-yl)ethoxy)-
1H-indol-2-ylmethylene]-4-(pyridin-4-yl)-1,3-dihydroindol-2-one
388116-60-7P 388116-61-8P 388116-62-9P
388116-64-1P 388116-65-2P 388116-66-3P
388116-68-5P 388116-70-9P, 3-(5-Methylthiophen-2-
ylmethylene)-4-(pyridin-4-yl)-1,3-dihydroindol-2-one 388116-73-2P
388116-74-3P 388116-76-5P 388116-79-8P
388116-80-1P, 3-[3-Methyl-4-((piperidin-1-yl)carbonyl)pyrrol-2-
vlmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
388116-81-2P, 3-[3-Methyl-4-(morpholine-4-carbonyl)pyrrol-2-
ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
388116-83-4P 388116-84-5P 388116-85-6P
388116-86-7P, 3-(3,5-Dimethyl-1H-pyrrol-2-ylmethylene)-4-
(piperidin-4-yl)-1,3-dihydroindol-2-one 388116-87-8P
388116-88-9P 388116-89-0P 388116-90-3P
388116-91-4P 388116-92-5P 388116-93-6P,
3-(1H-Indol-2-ylmethylene)-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
388116-94-7P, 4-(Piperidin-4-yl)-3-(4,5,6,7-tetrahydro-1H-indol-2-
ylmethylene)-1,3-dihydroindol-2-one 388116-95-8P,
3-[5-(2-(Morpholin-4-yl)ethoxy)-1H-indol-2-ylmethylene]-4-(piperidin-4-yl)-
1,3-dihydroindol-2-one 388116-96-9P 388116-97-0P
388116-98-1P, 3-[3-(3-Morpholin-4-ylpropyl)-4,5,6,7-tetrahydro-1H-
indol-2-ylmethylene]-4-(piperidin-4-yl)-1,3-dihydroindol-2-one
388116-99-2P 388117-00-8P, 3-[(3-Methyl-5-(4-
methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-4-(piperidin-4-yl)-1,3-
dihydroindol-2-one 388117-01-9P 388117-02-0P
388117-03-1P, 3-(5-Methylthiophen-2-ylmethylene)-4-(piperidin-4-
yl)-1,3-dihydroindol-2-one 388117-05-3P 388117-06-4P
388117-07-5P 388117-08-6P 388117-10-0P
388117-12-2P 388117-14-4P 388117-16-6P,
3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-
4-pyridin-2-yl-1, 3-dihydroindol-2-one 388117-17-7P,
3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-
4-pyrimidin-5-yl-1,3-dihydroindol-2-one 388117-18-8P,
3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-
4-(thiazol-2-yl)-1,3-dihydroindol-2-one 388117-19-9P
388117-20-2P 388117-21-3P 388117-22-4P,
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4-(6-Aminopyridin-3-yl)-3-[(3,5-dimethyl-4-(4-methylpiperazin-1-4ylcarbonyl)pyrrol-2-yl)methylene]-1,3-dihydroindol-2-one 388117-23-5P 388117-24-6P, 3-[(3,5-Dimethyl-4-(4methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-4-pyridin-3-yl-1,3dihydroindol-2-one 388117-25-7P 388117-26-8P, 5-[3-[(3,5-Dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2yl)methylene]-2-oxo-2,3-dihydro-1H-indol-4-yl]nicotinic acid **388117-27-9P**, 5-[3-[4-(2-Diethylaminoethylcarbamoyl)-3,5-dimethyl-1H-pyrrol-2-ylmethylene]-2-oxo-2,3-dihydro-1H-indol-4-yl]nicotinic acid 388117-28-0P 388117-29-1P, 4-(2-Aminopyrimidin-5-yl)-3-[(3,5-dimethyl-4-(4-methylpiperazin-1-ylcarbonyl)pyrrol-2-yl)methylene]-1,3-dihydroindol-2-one 388117-30-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug; prepn. and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones and their use as protein kinase inhibitors) 388116-44-7 CAPLUS RN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-CN vlidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-45-8 CAPLUS CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-1H-imidazol-4-yl)methylene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

RN 388116-46-9 CAPLUS
CN Pyrano[3,4-c]pyrrol-4(1H)-one, 1-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-6,7-dihydro- (9CI) (CA INDEX NAME)

RN 388116-47-0 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-50-5 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-(9CI) (CA INDEX NAME)

RN 388116-51-6 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridiny1)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-52-7 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-ethyl- (9CI) (CA INDEX NAME)

RN 388116-54-9 CAPLUS-

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & H & Me & \\ & HO_2C-CH_2-CH_2 & C-OEt \\ & & & \\ & & O & \\ \end{array}$$

RN 388116-55-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H \\ \hline & N & Me \\ \hline & CH_2-CH_2-CO_2H \\ \end{array}$$

RN 388116-56-1 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-57-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-pyridinyl)-(9CI) (CA INDEX NAME)

RN 388116-58-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(4-pyridinyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 388116-59-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[1H-indol-2-yl[2-(4-morpholinyl)ethoxy]methylene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

RN 388116-60-7 CAPLUS

CN 1H-Pyrrole-2-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-61-8 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-62-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[4-(4-morpholinyl)-1-(4,5,6,7-tetrahydro-1H-indol-2-yl)butylidene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

RN 388116-64-1 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-65-2 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-2-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-66-3 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 388116-68-5 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-phenyl-N-4-pyridinyl- (9CI) (CA INDEX NAME)

RN 388116-70-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-thienyl)methylene]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

RN 388116-73-2 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & O \\ \hline & H & C - OEt \\ \hline & HO_2C - CH_2 - CH_2 & Me \\ \hline & N & \end{array}$$

RN 388116-74-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

RN 388116-76-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-pyridinyl)-3H-indol-3-ylidene]methyl]-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 388116-79-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-1H-imidazol-4-yl)methylene]-4-(4-piperidinyl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 388116-78-7 CMF C18 H20 N4 O

2 CM

64-19-7 CRN CMF C2 H4 O2

RN

388116-80-1 CAPLUS
Piperidine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-CN ylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-81-2 CAPLUS

Morpholine, 4-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-iCNylidene]methyl]-4-methyl-1H-pyrrol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

RN 388116-83-4 CAPLUS

CN Pyrano[3,4-c]pyrrol-4(1H)-one, 1-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-6,7-dihydro-(9CI) (CA INDEX NAME)

RN 388116-84-5 CAPLUS

CN 4H-Pyrrolo[3,4-c]pyridin-4-one, 1-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 388116-85-6 CAPLUS

CN 4H-Pyrrolo[3,4-c]pyridin-4-one, 1-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,5,6,7-tetrahydro-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-86-7 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 388116-87-8 CAPLUS

CN 1H-Indole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

RN 388116-88-9 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-89-0 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-ethyl- (9CI) (CA INDEX NAME)

RN 388116-90-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(ethoxycarbonyl)-5-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & H & N & Me \\ \hline & HO_2C-CH_2-CH_2 & C-OEt \\ & & & O \\ \end{array}$$

RN 388116-91-4 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$^{\rm H}$$
  $^{\rm O}$   $^{\rm H}$   $^{\rm Me}$   $^{\rm CH_2-CH_2-CO_2H}$ 

RN 388116-92-5 CAPLUS

CN 1H-Pyrrole-3-acetic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388116-93-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-indol-2-ylmethylene)-4-(4-piperidinyl)-(9CI) (CA INDEX NAME)

RN 388116-94-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(4-piperidinyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]- (9CI) (CA INDEX NAME)

RN 388116-95-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-[1H-indol-2-y1[2-(4-morpholinyl)ethoxy]methylene]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 388116-96-9 CAPLUS
CN 1H-Pyrrole-2-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388116-97-0 CAPLUS
CN 1H-Pyrrole-3-carboxylic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-methyl- (9CI) (CA INDEX NAME)

RN 388116-98-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[4-(4-morpholinyl)-1-(4,5,6,7-tetrahydro-1H-indol-2-yl)butylidene]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 388116-99-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & Me \\ \hline & CH & N & Me \\ \hline & & C-NH-CH_2-CH_2-NEt_2 \\ \hline & & & O \\ \end{array}$$

RN 388117-00-8 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(4-piperidiny1)-3H-indol-3-ylidene]methyl]-4-methyl-1H-pyrrol-2-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-01-9 CAPLUS

CN 2H-Isoindole-1-carboxylic acid, 3-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-02-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-phenyl-N-4-pyridinyl-(9CI) (CA INDEX NAME)

RN 388117-03-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-methyl-2-thienyl)methylene]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 388117-05-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-5-(ethoxycarbonyl)-4-methyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O & H & O \\
 & CH & M & C-OEt \\
 & HO_2C-CH_2-CH_2 & Me & Me
\end{array}$$

RN 388117-06-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

RN 388117-07-5 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-08-6 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & H & \\ \hline & N & \\ & & CH & \\ & & N & \\ & & & C-NH-CH_2-Ph \\ & & & \\ & & & O \end{array}$$

RN 388117-10-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

RN 388117-12-2 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[1,2-dihydro-2-oxo-4-(4-piperidinyl)-3H-indol-3-ylidene]methyl]-4-methyl-N-[3-(2-oxo-1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)

RN 388117-14-4 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(2-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-16-6 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(2-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-17-7 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(5-pyrimidinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-18-8 CAPLUS

CN Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(2-thiazolyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-19-9 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(5-pyrimidinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-20-2 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(2-thiazolyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-21-3 CAPLUS

CN 1H-Pyrrole-3-carboxylic acid, 5-[[4-(6-amino-3-pyridinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 388117-22-4 CAPLUS

CN Piperazine, 1-[[5-[[4-(6-amino-3-pyridinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA

INDEX NAME)

RN

388117-23-5 CAPLUS
1H-Pyrrole-3-carboxylic acid, 5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2-methyl-4-[3-(4-methyl-1-piperazinyl)propyl]-, CN ethyl ester (9CI) (CA INDEX NAME)

RN

388117-24-6 CAPLUS
Piperazine, 1-[[5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA CN INDEX NAME)

RN 388117-25-7 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[3-[[4-(ethoxycarbonyl)-5-methyl-3-[3-(4-methyl-1-piperazinyl)propyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-4-yl]- (9CI) (CA INDEX NAME)

RN 388117-26-8 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[3-[[3,5-dimethyl-4-[(4-methyl-1-piperazinyl)carbonyl]-1H-pyrrol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-4-yl]- (9CI) (CA INDEX NAME)

09897755

RN 388117-27-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[3-[2-[[2-(diethylamino)ethyl]amino]-1-(3,5-dimethyl-1H-pyrrol-2-yl)-2-oxoethylidene]-2,3-dihydro-2-oxo-1H-indol-4-yl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & \\ \hline & NH-CH_2-CH_2-NEt_2 \\ \hline$$

RN 388117-28-0 CAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[[4-(2-amino-5-pyrimidinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-(diethylamino)ethyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

RN 388117-29-1 CAPLUS

CN Piperazine, 1-[[5-[[4-(2-amino-5-pyrimidinyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-2,4-dimethyl-1H-pyrrol-3-yl]carbonyl]-4-methyl- (9CI) (CA INDEX NAME)

RN 388117-30-4 CAPLUS

CN 1H-Pyrrole-3-carboxamide, N-[2-(diethylamino)ethyl]-5-[[1,2-dihydro-2-oxo-4-(3-pyridinyl)-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (9CI) (CA INDEX NAME)

IT 388116-49-2P, 3-(3,5-Dimethyl-1H-pyrrol-2-ylmethylene)-4-(pyridin-4-yl)-1,3-dihydroindol-2-one

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and use of 4-heteroaryl-3-heteroarylidenyl-2-indolinones and their use as protein kinase inhibitors)

RN 388116-49-2 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)

9

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PUBLISHER:

L5 ANSWER 5 OF 66 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:917070 CAPLUS

DOCUMENT NUMBER: 136:214530

TITLE: The t(8;22) in chronic myeloid leukemia fuses BCR to

FGFR1: transforming activity and specific inhibition

of FGFR1 fusion proteins

AUTHOR(S): Demiroglu, Asuman; Steer, E. Joanna; Heath, Carol;

Taylor, Kerry; Bentley, Mark; Allen, Steven L.; Koduru, Prasad; Brody, Judith P.; Hawson, Geoffrey; Rodwell, Robyn; Doody, Mary-Lou; Carnicero, Fernando; Reiter, Andreas; Goldman, John M.; Melo, Junia V.;

Cross, Nicholas C. P.

CORPORATE SOURCE: Department of Haematology, Imperial College School of

Medicine, Hammersmith Hospital, London, UK

SOURCE: Blood (2001), 98(13), 3778-3783 CODEN: BLOOAW; ISSN: 0006-4971

American Society of Hematology

DOCUMENT TYPE: Journal LANGUAGE: English

This report describes 2 patients with a clin. and hematol. diagnosis of chronic myeloid leukemia (CML) in chronic phase who had an acquired t(8;22)(p11;q11). Anal. by fluorescence in situ hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) indicated that both patients were neg. for the BCR-ABL fusion, but suggested that the BCR gene was disrupted. Further FISH indicated a breakpoint within fibroblast growth factor receptor 1 (FGFR1), the receptor tyrosine kinase that is known to be disrupted in a distinctive myeloproliferative disorder, most commonly by fusion to ZNF198. RT-PCR confirmed the presence in both cases of an in-frame mRNA fusion between BCR exon 4 and FGFR1 exon 9. Expression of BCR-FGFR1 in the factor-dependent cell line Ba/F3 resulted in interleukin 3-independent clones that grew at a comparable rate to cells transformed with ZNF198-FGFR1. The growth of transformed cells was inhibited by the phosphatidylinositol 3-kinase inhibitor LY294002, the farnesyltransferase inhibitors L744832 and manumycin A, the p38 inhibitors SB202190 and SB203580 but not by the MEK inhibitor PD98059. The growth of BaF3/BCR-FGFR1 and BaF3/ZNF198-FGFR1 was not significantly inhibited by treatment with STI571, but was inhibited by SU5402, a compd. with inhibitory activity against FGFR1. Inhibition with this compd. was assocd. with decreased phosphorylation of ERK1/2 and BCR-FGFR1 or ZNF198-FGFR1, and was dose dependent with an inhibitory concn. of 50% of approx. 5 .mu.M. As expected, growth of BaF3/BCR-ABL was inhibited by STI571 but not by SU5402. The study demonstrates that the BCR-FGFR1 fusion may occur in patients with apparently typical CML. Patients with constitutively active FGFR1 fusion genes may be amenable to treatment with specific FGFR1 inhibitors.

r **215543-92-3**, SU 5402

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(t(8;22) in chronic myeloid leukemia fuses BCR to FGFR1: transforming activity and specific inhibition of FGFR1 fusion proteins)

RN 215543-92-3 CAPLUS

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 66 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:905718 CAPLUS

DOCUMENT NUMBER: 136:160779

TITLE: Semaxanib (SUGEN)
AUTHOR(S): Sakamoto, Kathleen M.

CORPORATE SOURCE: Department of Pedlatncs and Pathology, UCLA School of

Medicine, Los Angeles, CA, 90095-1752, USA

SOURCE: IDrugs (2001), 4(9), 1061-1067

CODEN: IDRUFN; ISSN: 1369-7056

PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review. SUGEN (owned by Pharmacia) is developing semaxanib (SU-5416), the lead in a series of small mol. inhibitors of the flk-1 tyrosine kinase receptor (flk-1 RTK), for the potential treatment of solid tumors (via suppression of metastasis and angiogenesis). In July 1999, phase III trials for colorectal and lung cancer were initiated. In Mar. 2001, phase III trials were initiated for the compd. as an addn. to a std. chemotherapy regimen in colorectal cancer; at this time, Pharmacia, as well as the NCI, was conducting clin. studies for numerous other solid and hematol. cancers. By Oct. 2000, oral forms of the compd. were also being evaluated. In July 2000, Pharmacia anticipated US and international filing in 2001. Taiho and SUGEN have agreed a joint development program for SUGEN's angiogenesis inhibitors. In August 1998, the USPTO issued US-05792783 to SUGEN, covering a family of compds., including semaxanib. The patent claims cover the compds. and compn., as well as methods of use in a variety of diseases, including cancer. In August 1998, the USPTO issued US-05792783 to SUGEN, covering a family of compds., including semaxanib. The patent claims cover the compds. and compn., as well as methods of use in a variety of diseases, including cancer.

IT 194413-58-6, Semaxanib

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(semaxanib, an inhibitor of the flk-1 tyrosine kinase receptor, for potential treatment of solid tumors in humans)

RN 194413-58-6 CAPLUS

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

39

L5ANSWER 7 OF 66 CAPLUS COPYRIGHT 2002 ACS 2001:904107 CAPLUS ACCESSION NUMBER:

136:37505 DOCUMENT NUMBER:

Preparation of 3-(2-indolylmethylene)-2-indolinones as TITLE:

protein kinase/phosphatase inhibitors for treatment of

THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS

proliferative diseases

Tang, Peng Cho; Harris, G. Davis; Li, Xiaoyuan INVENTOR(S):

Sugen, Inc., USA PATENT ASSIGNEE(S):

PCT Int. Appl., 199 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

REFERENCE COUNT:

PATENT NO.				KIND		DATE			APPLICATION NO.					DATE			
WC	2001	2001094312			 2	20011213			WO 2001-US17961					20010604			
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
														GB,			
														ΚZ,			
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NΖ,	PL,	PT,
														TZ,			
														ТJ,			
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪG,	ZW,	AT,	BE,	CH,	CY,
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
														TD,			
បន	2002	Α	1	20020502				US 2001-871700				20010604					
PRIORITY APPLN. INFO.								1	US 2	000-	2091	62P	P	2000	0602		
OTHER SOURCE(S):				MARPAT 136:37505													

GI

$$\begin{array}{c|c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ &$$

Title compds. I [wherein R4-R6 and R8-R10 = H; R1, R2, and R3 = AB independently H, halo, carboxylic acid, trihalomethyl, or (un) substituted ester, amide, alkyl, alkoxy, or (hetero)aryl; R7 = (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salt thereof] were prepd. as modulators of the activity of protein kinases (PKs) and phosphatases. For example, 5-bromo-2-oxindole was coupled with 5-(3-diethylaminopropyl)-1Hindole-2-carbaldehyde (prepn. given) in the presence of piperidine in EtOH to afford II, which inhibited GST-FLK-1, EGF receptor kinase, and PDGF with IC50 values of 0.03 .mu.M, 2.87 .mu.M, and 0.38 .mu.M, resp. I are useful in treating disorders related to abnormal PK activity, such as blood vessel proliferative disorders, mesangial cell proliferative disorders, fibrotic disorders, cancer, diabetes, autoimmune disorders, hyperproliferation disorders, restenosis, fibrosis, psoriasis, von Heppel-Lindau disease, osteoarthritis, rheumatoid arthritis, angiogenesis, inflammatory disorders, immunol. disorders, and cardiovascular disorders (no data). Combinatorial libraries comprising at least five indolinone compds., formed by reacting oxindoles with aldehydes, are also claimed.

ΙI

Ι

## IT 258830-88-5P

RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

RN 258830-88-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N,N-dimethyl-2-oxo-(9CI) (CA INDEX NAME)

$$Me_2N - S$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

## IT 258830-79-4P 258830-86-3P 380241-29-2P

380241-30-5P 380241-31-6P 380241-33-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

RN 258830-79-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-86-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[(2-methyl-1H-indol-3-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & Me_2N - S & CH \\
 & O & Me & H
\end{array}$$

RN 380241-29-2 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

Br 
$$CH$$
  $N$   $O$   $O-CH_2-CH_2-NEt_2$ 

RN 380241-30-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)

RN 380241-31-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

Ph 
$$CH \longrightarrow CH_2 - CH_2 - NEt_2$$

RN 380241-33-8 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

TT 258830-66-9P 380242-44-4P 380242-45-5P 380242-46-6P 380242-47-7P 380242-48-8P 380242-49-9P 380242-50-2P 380242-51-3P 380242-52-4P 380242-53-5P 380242-54-6P 380242-55-7P 380242-56-8P 380242-57-9P 380242-58-0P 380242-69-1P 380242-60-4P 380242-61-5P 380242-62-6P 380242-63-7P 380242-64-8P 380242-65-9P 380242-66-0P 380242-67-1P 380242-68-2P 380242-69-3P 380242-70-6P 380242-71-7P 380242-72-8P 380242-73-9P 380363-16-6P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

RN 258830-66-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ H_2N - S & & \\ & & \\ & & \\ & & \\ \end{array}$$

RN 380242-44-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N,N-dimethyl-2-oxo-(9CI) (CA INDEX NAME)

$$Me_2N - S$$

$$0$$

$$0$$

$$N$$

$$H$$

$$O$$

$$O$$

$$N$$

$$H$$

$$O$$

$$O$$

$$N$$

$$H$$

RN 380242-45-5 CAPLUS

CN Piperazine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]-4-methyl-(9CI) (CA INDEX NAME)

RN 380242-46-6 CAPLUS

CN Pyrrolidine, 1-[[3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-1H-indol-5-yl]sulfonyl]- (9CI) (CA INDEX NAME)

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RN 380242-47-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyethyl)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-48-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 380242-49-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-N-(2-methoxyphenyl)-2-oxo- (9CI) (CA INDEX NAME)

RN 380242-50-2 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

C1 
$$NH-S$$
  $CH-NH-S$   $CH-N$ 

RN 380242-51-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-N-[(4-fluorophenyl)methyl]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

F

$$CH_2-NH-S$$
 $CH_2-NH-S$ 
 $CH_2-NH-S$ 
 $CH_2-NH-S$ 
 $CH_2-NH-S$ 
 $CH_3-NEt_2$ 

RN 380242-52-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & H_2N - S & H \\
 & O & H \\
 & O & H
\end{array}$$

380242-53-5 CAPLUS RN

1H-Indole-5-sulfonamide, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-CN yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
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RN 380242-54-6 CAPLUS

1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-N-CN (phenylmethyl) - (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{Ph-CH}_2-\text{NH-S} & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN

380242-55-7 CAPLUS
Pyrrolidine, 1-[[2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-1H-indol-5-CN yl]sulfonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 380242-56-8 CAPLUS

1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-CN methoxyethyl)-2-oxo- (9CI) (CA INDEX NAME)

$$MeO-CH_2-CH_2-NH-S$$

$$O$$

$$O$$

$$CH$$

$$H$$

$$O$$

$$H$$

RN 380242-57-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(2-methoxyphenyl)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-58-0 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-59-1 CAPLUS

CN 1H-Indole-5-sulfonamide, N-[(4-fluorophenyl)methyl]-2,3-dihydro-3-(1H-indol-2-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} F & & & & \\ \hline \\ CH_2-NH-S & & & \\ \hline \\ O & & & \\ \end{array}$$

RN 380242-60-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-2-ylmethylene)-N-(1-methylethyl)-2-oxo- (9CI) (CA INDEX NAME)

RN 380242-61-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 380242-62-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

MeO 
$$CH_2$$
  $CH_2$   $CH_2$   $CH_2$   $NEt_2$ 

RN 380242-63-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)

RN 380242-64-8 CAPLUS

CN 1H-Indole-4-carboxylic acid, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI) (CA INDEX NAME)

RN 380242-65-9 CAPLUS

CN 2H-Indol-2-one, 6-bromo-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 380242-66-0 CAPLUS

CN 1H-Indole-4-carboxamide, N-(3-chloro-4-methoxyphenyl)-3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-2,3-dihydro-2-oxo-(9CI)(CA INDEX NAME)

RN 380242-67-1 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$N-(CH_2)_3$$
 $N$ 
 $CH$ 
 $CH_2$ 
 $CO_2$ 
 $CO_2$ 

RN 380242-68-2 CAPLUS

CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & O \\
 & \parallel \\
 & C-NH-CH_2-CO_2H \\
\hline
 & O \\
 & \parallel \\
 & C-NH-CH_2-CO_2H \\
\end{array}$$

RN 380242-69-3 CAPLUS

CN Glycine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H \\
 & N \\
 & O \\
 & M \\
 & O \\
 & M \\
 & O \\$$

RN 380242-70-6 CAPLUS

CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$(CH_2)_3$$

$$0$$

$$N$$

$$H$$

$$S$$

$$CO_2H$$

RN 380242-71-7 CAPLUS

CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 380242-72-8 CAPLUS

CN L-Alanine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 380242-73-9 CAPLUS

CN L-Valine, N-[[2,3-dihydro-2-oxo-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]-1H-indol-6-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$(CH_2)_3$$

$$0$$

$$M$$

$$N$$

$$O$$

$$CO_2H$$

RN 380363-16-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-(pyridinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{D1} & \overset{H}{\text{N}} & \text{O} \\ \text{CH} & \overset{N}{\text{H}} \end{array}$$

## IT 380242-01-3P

RL: CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

RN 380242-01-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[(4-methoxy-1H-indol-2-yl)methylene]-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

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ΙT
    181223-16-5P 203988-69-6P 215543-45-6P
    258830-80-7P 258830-85-2P 258830-87-4P
    258830-90-9P 258830-91-0P 380241-13-4P
    380241-14-5P 380241-15-6P 380241-16-7P
    380241-17-8P 380241-18-9P 380241-19-0P
    380241-20-3P 380241-21-4P 380241-22-5P
    380241-23-6P 380241-24-7P 380241-25-8P
    380241-26-9P 380241-27-0P 380241-28-1P
    380241-32-7P 380241-34-9P 380241-35-0P
    380241-36-1P 380241-37-2P 380241-38-3P
     380241-39-4P 380241-40-7P 380241-41-8P
    380241-42-9P 380241-43-0P 380241-44-1P
    380241-45-2P 380241-46-3P 380241-47-4P
    380241-48-5P 380241-49-6P 380241-50-9P
    380241-51-0P 380241-53-2P 380241-54-3P
    380241-56-5P 380241-59-8P 380241-61-2P
    380241-65-6P 380241-68-9P 380241-71-4P
     380241-74-7P 380241-78-1P 380241-82-7P
     380241-84-9P 380241-86-1P 380241-88-3P
     380241-90-7P 380241-91-8P 380241-92-9P
    380241-93-0P 380241-94-1P 380241-95-2P
    380241-96-3P 380241-97-4P 380241-98-5P
    380241-99-6P 380242-00-2P
```

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)indolinones as protein kinase/phosphatase inhibitors for treatment of proliferative diseases)

181223-16-5 CAPLUS

1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-2-oxo-CN (CA INDEX NAME)

$$\begin{array}{c|c}
& & & \\
& & & \\
H_2N - S & & \\
& & & \\
& & & \\
\end{array}$$

RN203988-69-6 CAPLUS 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-N-methyl-2-CN oxo- (9CI) (CA INDEX NAME)

RN 215543-45-6 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[(2-methyl-1H-indol-3-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

RN 258830-80-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-5-ylmethylene)-N-methyl-2-oxo- (9CI) (CA INDEX NAME)

RN 258830-85-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-5-ylmethylene)-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

$$Me_2N - S$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

RN 258830-87-4 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-5-ylmethylene)-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ H_2N - S & \\ & & \\ & & \\ O & \\ \end{array}$$

RN 258830-90-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-(1H-indol-3-ylmethylene)-N,N-dimethyl-2-oxo-(9CI) (CA INDEX NAME)

$$Me_2N - S$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

$$0$$

RN 258830-91-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[(2-methyl-1H-indol-3-yl)methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$H_2N-S$$
 $O$ 
 $Me$ 
 $N$ 
 $Me$ 
 $N$ 

RN 380241-13-4 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 380241-14-5 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

Br 
$$CH \longrightarrow N$$
  $CH \longrightarrow N$   $H$   $CH_2)_3-NEt_2$ 

RN 380241-15-6 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl-(9CI) (CA INDEX NAME)

RN 380241-16-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[3-(diethylamino)propyl]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl-(9CI) (CA INDEX NAME)

RN 380241-17-8 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-5-phenyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & CH_2-CH_2-NMe_2 \\ \hline Ph & H & \end{array}$$

RN 380241-18-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-19-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \hline \\ O & & \\ \end{array}$$

RN 380241-20-3 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H \\ N \\ \hline \\ O \\ \end{array} \\ \begin{array}{c} H \\ N \\ \end{array} \\ \begin{array}{c} CH \\ \hline \\ O \\ H \\ \end{array} \\ \begin{array}{c} Br \\ \end{array}$$

RN 380241-21-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-22-5 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 380241-23-6 CAPLUS

CN 2H-Indol-2-one, 5-bromo-3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 380241-24-7 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(dimethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-6-phenyl- (9CI) (CA INDEX NAME)

Ph 
$$CH \longrightarrow CH \longrightarrow CH_2 - CH_2 - NMe_2$$

RN 380241-25-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & &$$

RN 380241-26-9 CAPLUS

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-27-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-28-1 CAPLUS

CN 2H-Indol-2-one, 3-[[5-[2-(diethylamino)ethoxy]-1H-indol-2-yl]methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O & O-CH_2-CH_2-NEt_2 \\ \hline \\ CH & N & H \end{array}$$

RN 380241-32-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[3-(1-pyrrolidinyl)propyl]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-34-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-35-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-36-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & CH_2-CH_2-OH \\ \hline & N-CH_2-CH_2-O \\ \hline & N-CH_2-CH_2-OH \\ \hline \end{array}$$

RN 380241-37-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-pyridinyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-38-3 CAPLUS

©CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(1-

pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-39-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-40-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-41-8 CAPLUS

CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-42-9 CAPLUS

CN 1H-Indole-5-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$N - CH_2 - CH_2 - O$$
 $N - CH_2 - CH_2 - O$ 
 $N - CH_2 - CH_2 - O$ 

RN 380241-43-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-44-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-y1]methylene]-5-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-45-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-4-(2-hydroxyethyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & CH_2-CH_2-OH \\ \hline \\ N-CH_2-CH_2-O \\ \hline \\ O \\ N \\ H \end{array}$$

RN 380241-46-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-6-(3-pyridinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
H & O \\
N & CH & N \\
H & CH & N \\
H & CH & N \\
\end{array}$$

RN 380241-47-4 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(4-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-48-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(3-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & O \\ \hline \\ MeO \end{array} \begin{array}{c} H & O \\ \hline \\ CH & M \end{array} \begin{array}{c} O - CH_2 - CH_2 - M \\ \hline \\ \end{array}$$

RN 380241-49-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

OMe 
$$H$$
  $O$   $CH_2-CH_2-N$   $O$ 

RN 380241-50-9 CAPLUS

CN 2H-Indol-2-one, 6-(4-fluorophenyl)-1,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

F 
$$O-CH_2-CH_2-N$$

RN 380241-51-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-53-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 380241-54-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-56-5 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-59-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-61-2 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-phenyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

RN 380241-65-6 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-2-oxo-N-3-pyridinyl-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA'INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ N - CH_2 - CH_2 - O \end{array}$$

RN 380241-68-9 CAPLUS

CN 1H-Indole, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro-(9CI) (CA INDEX NAME)

$$O = S$$

$$CH = CH_2 - CH_2 - N$$

RN 380241-71-4 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

PAGE 1-B

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RN 380241-74-7 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ N - CH_2 - CH_2 - O \end{array}$$

RN 380241-78-1 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

PAGE 1-B

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RN 380241-82-7 CAPLUS

Quinoline, 1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro-(9CI) (CA INDEX NAME)

$$O = S$$

$$O = S$$

$$O = S$$

$$O = CH_2 - CH_2 - N$$

$$H$$

RN 380241-84-9 CAPLUS

CN Isoquinoline, 2-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

RN 380241-86-1 CAPLUS

CN 1H-Indole, 5-bromo-1-[[2,3-dihydro-2-oxo-3-[[5-[2-(1-pyrrolidinyl)ethoxy]-1H-indol-2-yl]methylene]-1H-indol-5-yl]sulfonyl]-2,3-dihydro-(9CI) (CA INDEX NAME)

Br 
$$O = S$$
  $CH = N$   $O = CH_2 - CH_2 - N$ 

RN 380241-88-3 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O \\ H & N \\ \hline O & N \\ \hline$$

RN 380241-90-7 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ H \\ N \\ CH \\ CH_2 - CH_2 - O \end{array}$$

RN 380241-91-8 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N-(1-methylethyl)-3-[[5-[2-(4-

morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 380241-92-9 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O \\ \parallel & \\ N-CH_2-CH_2-O \end{array}$$

RN 380241-93-0 CAPLUS

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-N-3-pyridinyl- (9CI) (CA INDEX NAME)

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RN 380241-94-1 CAPLUS

CN 1H-Indole, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & H & O \\
 & N & H & O \\
 & O & CH_2 - CH_2 - N & O
\end{array}$$

RN 380241-95-2 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

$$-N$$

RN 380241-96-3 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(3-chlorophenyl)-2,3-dihydro-N-methyl-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me O} & \\ & \text{N} & \\ & \text{N} & \\ & \text{O} & \\ & & \text{CH} & \\ & & \text{N} & \\ & & \text{H} & \\ \end{array}$$

RN 380241-97-4 CAPLUS

CN 1H-Indole-5-sulfonamide, N-(4-chloro-2-fluorophenyl)-2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-(9CI) (CA INDEX NAME)

PAGE 1-A

$$\begin{array}{c|c} C1 & O & H & O \\ \hline & NH - S & CH & H \\ \hline & O & H \\ \hline \end{array}$$

PAGE 1-B

$$-N$$

RN 380241-98-5 CAPLUS

CN Quinoline, 1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-

yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

$$O = S$$

$$CH = N$$

$$N$$

$$H$$

$$O = CH_2 - CH_2 - N$$

RN 380241-99-6 CAPLUS

CN Isoquinoline, 2-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-1,2,3,4-tetrahydro-(9CI) (CA INDEX NAME)

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RN 380242-00-2 CAPLUS

CN 1H-Indole, 5-bromo-1-[[2,3-dihydro-3-[[5-[2-(4-morpholinyl)ethoxy]-1H-indol-2-yl]methylene]-2-oxo-1H-indol-5-yl]sulfonyl]-2,3-dihydro-(9CI) (CA INDEX NAME)

Br 
$$O = S$$
  $CH = N$   $O = CH_2 - CH_2 - N$   $O = CH_2 - CH_2 - N$ 

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ACCESSION NUMBER:

2001:830898 CAPLUS

DOCUMENT NUMBER:

135:357926

TITLE:

Synthesis of indolinone vinyl-derivatives used to

modulate protein kinase activity

INVENTOR(S):

Tang, Peng Cho; Sun, Li; Mcmahon, Gerald; Harris, G.

David

PATENT ASSIGNEE(S):

Sugen, Inc., USA

SOURCE:

U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 212,494.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

## PATENT INFORMATION:

PATENT NO.			KIN	ID	DATE				APP	LIC	AT:	ION	NC	). 	DATE				
US	US 6316635				B1		20011113				199					1999			
US	JS 5880141			Α		19990309										1995			
US	5 5792783			Α		19980811					199					1996			
US	5883113			Α		19990316					199				_	1996			
EP	934931			A2		19990811				EΡ	199	9-	103	667	7	1996	0605		
EP	934931					19991020													
	R: 7	ΑT,	BE,	CH,	DE,	, DK,	ES,	FR,	GB	, G	R,	IT	, I	ıΙ,	LU,	NL,	SE,	MC,	PT,
						, FI													
JP	P 2000026412									JР	199	9-	159	56	7	1996			
				B1												1998			
US 2001027207			A.	L	2001	1004									2001				
US 2002028840			A.	l	2002	0307									2001				
PRIORITY APPLN. INFO.			. :												1995				
											95-4					1995			
								τ	JS	199	6-6	555	223	3		1996			
								τ	IJS	199	6-6	559	191	L		1996			
											8-8				P				
								1	US	199	8-2	212	494	1		1998			
								]	EΡ	199	96-9	918	093	3		1996			
									JP	199	97-5	501	363	3		1996			
								1	US	199	9-2	293	518	3	A1	1999	0415		
OTHER SOURCE(S):			MARPAT 135:				3579	26											

GΙ

$$R^7$$
 $R^8$ 
 $R^9$ 
 $R^1$ 
 $R^3$ 
 $R^4$ 
 $R^5$ 
 $R^5$ 

I

Title compds. I [G, J = N such that, when G = N, J = C and when J = N, G = C, it being recognized that, when G or J = N, R5 or R5' does not exist; R1-3 = H; R4, R5, R5' H, alk(en/yn)yl, cycloalkyl, aryl, heteroaryl, heteroalicylic, halo, hydroxy, nitro, cyano, alkoxy, aryloxy, etc.; R6-9 = AΒ

H, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, etc.] with some exceptions, were prepd. For instance, 2-ethyl-4-formylimidazole was reacted with resin bound 2-chlorotriphenylmethyl chloride (CH2Cl2, iPr2NEt, 21 h, room temp.) and the isolated product condensed with 2-indolinone (DMF, piperidine, 80.degree.C, 20 h) to give the corresponding resin-bound 2-indolinone. The resin bound intermediate was cleaved (CH2Cl2, TFA, 2 h, room temp.) to give II as the TFA salt of a 10:1 E/Z mixt. I exhibit kinase inhibitory activity and are useful for treating, e.g., diabetes, autoimmune disorder, etc.

ΙT 186611-44-9P, 3-[(Imidazol-4-yl)methylene]-2-indolinone 204006-26-8P, 3-[(Imidazol-4-yl)methylene]-4,6-dimethyl-2indolinone 204006-35-9P, 3-[(Imidazol-4-yl)methylene]-5-chloro-2indolinone 215434-21-2P, 3-[(Imidazol-4-yl)methylene]-5-nitro-2indolinone 215434-22-3P, 3-[(Imidazol-4-yl)methylene]-5-fluoro-2indolinone 215434-43-8P, 3-[(Imidazol-4-yl)methylene]-5-amino-2indolinone 215434-63-2P, 3-[(Imidazol-4-yl)methylene]-5,6dimethoxy-2-indolinone 245036-30-0P, 3-[(Imidazol-4yl)methylene]-4-methyl-2-indolinone 245036-31-1P, 3-[(Imidazol-4-yl)methylene]-5-chloro-7-bromo-2-indolinone RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug; synthesis of indolinone vinyl-derivs. used to modulate protein kinase activity) 186611-44-9 CAPLUS RN

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

RN 204006-26-8 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-4,6-dimethyl(9CI) (CA INDEX NAME)

RN 204006-35-9 CAPLUS CN 2H-Indol-2-one, 5-chloro-1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

215434-21-2 CAPLUS RN

2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-5-nitro- (9CI) CN(CA INDEX NAME)

$$O_2N$$
 $H$ 
 $O_1$ 
 $O_2$ 
 $O_3$ 
 $O_4$ 
 $O_4$ 
 $O_5$ 
 $O_5$ 
 $O_7$ 
 $O_8$ 
 $O_8$ 

215434-22-3 CAPLUS RN

2H-Indol-2-one, 5-fluoro-1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) CN (CA INDEX NAME)

$$\begin{array}{c|c} & H & O & H \\ \hline & CH & N \\ \end{array}$$

215434-43-8 CAPLUS RN

2H-Indol-2-one, 5-amino-1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) CN (CA INDEX NAME)

$$H_{2N}$$
 $H_{2N}$ 
 $H_{2N}$ 
 $H_{2N}$ 
 $H_{2N}$ 
 $H_{2N}$ 

215434-63-2 CAPLUS RN

2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-5,6-dimethoxy-CN(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{MeO} \\ \\ \text{MeO} \\ \end{array}$$

RN 245036-30-0 CAPLUS

2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-4-methyl- (9CI) CN (CA INDEX NAME)

RN 245036-31-1 CAPLUS

CN 2H-Indol-2-one, 7-bromo-5-chloro-1,3-dihydro-3-(1H-imidazol-4-ylmethylene)(9CI) (CA INDEX NAME)

$$C1 \xrightarrow{\operatorname{Br}} \overset{H}{\overset{H}{\overset{}}} \circ CH \xrightarrow{\overset{H}{\overset{}}} \overset{H}{\overset{}}$$

## IT 372164-79-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (intermediate; synthesis of indolinone vinyl-derivs. used to modulate protein kinase activity)

RN 372164-79-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

## IT 186611-44-9DP, polymer-bound 372164-72-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; synthesis of indolinone vinyl-derivs. used to modulate protein kinase activity)

RN 186611-44-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)- (9CI) (CA INDEX NAME)

RN 372164-72-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-imidazol-4-ylmethylene)-, (3E)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 372164-71-1 CMF C12 H9 N3 O

Double bond geometry as shown.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

REFERENCE COUNT:

THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT